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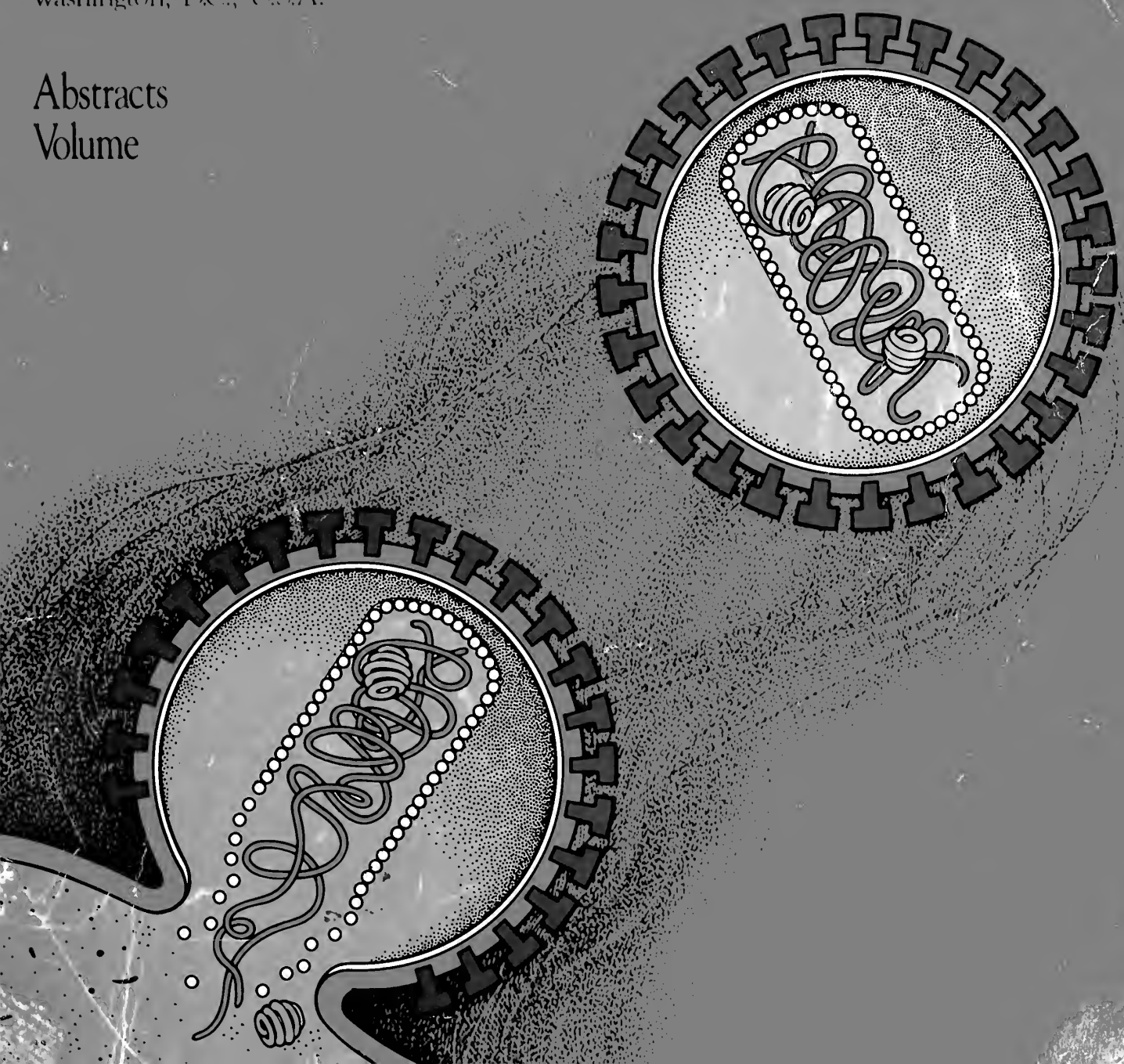
AIDS

June 1-5, 1987
Washington Hilton Hotel
Washington, DC., U.S.A.

Abstracts Volume



III INTERNATIONAL CONFERENCE ON ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

June 1-5, 1987
Washington Hilton and Towers
Washington, D.C.

The purpose of the conference is to review and exchange information on AIDS epidemiology, virology, molecular biology, immunology, serology, hematology, animal models, neurological implications, neuropsychiatric aspects, oncology, diagnostic tests, clinical manifestations, behavioral and addiction aspects, public health, ethical and psychosocial implications, and prevention and control strategies.

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Opening Plenary Session

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General Introductory, Welcoming and Keynote Remarks

Speakers include:

The Honorable George Bush, Vice President of the United States

Robert E. Windom, Assistant Secretary for Health, U.S. Department of Health and Human Services, Washington, D.C.

C. Everett Koop, Surgeon General and Director of the International Health Program Office, U.S. Public Health Service, Washington, D.C.

Lowell T. Harmison, Deputy Assistant Secretary for Health, U.S. Department of Health and Human Services, Washington, D.C.

Carlyle Guerra de Macedo, Director, Pan American Health Organization, Washington, D.C.

George J. Galasso, General Chairman, III International Conference on AIDS and Associate Director for Extramural Affairs, National Institutes of Health, Bethesda, Maryland.

Plenary Session I

M.2.1 The AIDS Viruses

Robert Gallo, National Cancer Institute, National Institutes of Health, Washington, D.C.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

M.2.2 Significance of variation between human immunodeficiency (HIV) isolates for serology and vaccine development.

ERLING NORRBY*, GUNNEL BIBERFELD*, JAN ALBERT*,***, FRANCESCA CHIODI*, KRISTINA LJUNGGREN*,****, EVA-MARIA FENYO*, *Dept. Virology, Karolinska Institute, **Dept. Immunology and *** Dept. Virology, National Bacteriological Laboratory, and ****Dept. Immunology, Karolinska Institute, Stockholm, Sweden.

Two groups of HIVs have been identified. The group of HIVs isolated from West Africans includes the strains HTLV-4, LAV-2 and SBL-6669. These strains have closely related envelope glycoproteins, which differ markedly from the corresponding proteins of HIVs represented by the strain HTLVIIIB. This difference is reflected in distinctive reactions in antibody-dependent cell cytotoxicity of antibodies against HIV and the HIV-related West African virus isolates. The internal components of HIVs of both groups share immunogenic properties, but certain distinguishing features have been identified. The occurrence of the two groups of HIVs need to be considered in development of accurate and sensitive serological tests and in attempts to introduce effective immunoprophylactic measures. Site-directed serology using synthetic peptides offers attractive possibilities for establishment of serological tests which can distinguish antibody responses to viruses representing the two groups of HIVs.

M.2.3 The natural history and clinical manifestations of HIV-infection

PETER PIOT. Institute of Tropical Medicine, Antwerp, Belgium.

The clinical expression of HIV-infection appears increasingly complexe. It includes manifestations due to opportunistic diseases, as well as illness directly caused by HIV itself. Neurological disease may include involvement of brain, spinal cord and peripheral nerves, and is probably directly caused by HIV, as is lymphocytic interstitial pneumonia. The etiology of chronic diarrhea and a papular pruritic skin eruption associated with HIV-infection is unclear. Several clinical classification systems for HIV-infection have ben proposed. Between 2 and 8 % of infected individuals per year progress to AIDS, with no apparent decrease in the rate of disease progression over time. Within 5 to 10 years of infection the majority of infected persons develop clinical disease. Reported risk factors and/or predictors of disease progression such as a decreased number of T-helper lymphocytes, an increased number of T-suppressor lymphocytes, a low level of HIV-antibody and a high titer of CMV-antibody, may be markers or reflect duration of infection. A chronically activated state secondary to chronic viral and parasitic antigenic exposure may increase both the susceptibility to HIV-infection and development of disease. Increased HIV gene expression and persistent antigenemia may also be contributing factors in disease development. Persistent viral production in monocyte/macrophage cells in the brain and elsewhere may be a source of virus production in other organs. Infection of the brain implies that HIV may be protected from immune surveillance or therapeutic intervention.

Epidemiology—Natural History

M.3.1 The Natural History of Human Immunodeficiency Virus Infection in a Cohort of Homosexual and Bisexual Men: a 7-year Prospective Study.

NANCY A. HESSOL*, GW RUTHERFORD*, PM O'MALLEY*, LS DOLL**, WW DARROW**, HW JAFFE**, et al., *Dept.of Public Health, San Francisco, CA, and Centers for Disease Control, Atlanta, GA.

To determine the natural history of HIV infection, a stratified random sample of 6,700 homosexual and bisexual men originally recruited between 1978 and 1980 for studies of hepatitis B were evaluated. To date, 662 (9.9%) of these men have been reported with AIDS, and approximately 70% are estimated to be infected with HIV. Of the 719 (11%) men randomly chosen from the entire cohort who participated in AIDS studies, 63 were known to have seroconverted before the studies began in late 1983. These 63 men have now been followed for a mean of 72 months since their initial seropositive specimen or estimated date of seroconversion: 19 (30%) have been reported to have AIDS; 29 (46%) had generalized lymphadenopathy, oral candidiasis, weight loss, persistent idiopathic fever or diarrhea; and 15 (24%) were asymptomatic. Additional data were analyzed from 273 men who participated in hepatitis B vaccine trials, for whom multiple serum specimens were available, and who consented to have their old serum specimens tested for the presence of HIV antibodies. Of these 273 men, 112 (41%) were either seropositive on entry into the cohort (18 men) or had known seroconversion dates within a 24 month period (94 men). Combining these 112 men with the 63 men from the random sample, a Kaplan-Meier survival curve of the cumulative proportion of men without AIDS by duration of HIV infection was constructed. From analysis of these 155 men, an estimated 15% (95% confidence interval, 9 - 21%) of the HIV infected men in the Clinic cohort will develop AIDS over 60 months of infection, 24% (95% c.i., 17 - 31%) will develop AIDS after 72 months, 31% (95% c.i., 22 - 40%) will develop AIDS after 84 months, and 36% (95% c.i., 26 - 46%) after 88 months.

M.3.2 In a Cohort of HIV Seropositive Men Followed for 30 Months, Initial Leu 3a T Lymphocyte Counts Predict Subsequent Declines in T Cell Counts, Clinical Findings and AIDS

WILLIAM LANG*, R. ANDERSON**, W. WINKELSTEIN, Jr.***, R. ROYCE***, H. PERKINS****, *Children's Hospital of San Francisco, CA, **California Department of Health Services, Sacramento, CA, ***UCB School of Public Health, Berkeley, CA, ****Irwin Memorial Blood Bank, San Francisco, CA.

From the San Francisco Men's Health Study, a prospective study of HIV infection in a population-based probability sample, 370 HIV-infected men were recruited. A subset of 206 men attended examinations every 6 months from June 1984 through December 1986. Initial Leu 3a counts were unimodally distributed and depressed compared to uninfected men. Over 30 months, the entire distribution shifted toward lower values. When the group was stratified according to initial Leu 3a count, declines of 18 to 30% occurred in all quartiles indicating depletion of Leu 3a cells regardless of initial values.

To explore the relationship of initial Leu 3a values to development of HIV related symptoms and AIDS, all 370 seropositive men were stratified into groups with less than 500 (n=100), 500-650 (n=92), 650-800 (n=81), and greater than 800 (n=97) initial Leu 3a cells. Among participants with less than 2 symptoms suggestive of HIV infection at outset, 25% with less than 500 Leu 3a cells developed increasing symptoms compared to 12% of those with greater than 800 Leu 3a cells. Twenty-four of the 37 AIDS cases occurred in the lowest group compared to 5 in the highest.

These findings suggest that HIV infection affects Leu 3a counts progressively in most people and that initial Leu 3a number is strongly predictive of clinical outcome in the ensuing 30 months.

M.3.3 Progression to AIDS, predictors of AIDS, and seroconversion in a cohort of homosexual men: Results of a four year prospective study.

MARTIN T SCHECHTER, WJ BOYKO, MS WEAVER, B DOUGLAS, B WILLOUGHBY, WA MCLEOD, et al. The Vancouver Lymphadenopathy-AIDS Study, St. Paul's Hospital, University of British Columbia, Vancouver, BC, Canada.

The Vancouver Lymphadenopathy-AIDS Study is an ongoing prospective study of over 600 homosexual men who were recruited through their GP's beginning in 11/82 and who have been seen since at roughly six-month intervals. A total of 323 men were seropositive at entry into the study. Through 11/86, a total of 36 cases of AIDS were diagnosed in this group, yielding a Kaplan-Meier (K-M) estimate for the 48 month cumulative incidence of AIDS of 18.6%. The following are the categories (and K-M estimates of the four-year incidence of AIDS) for the lab predictors of progression to AIDS:

CD4 count	<400 (33.6%)	CD4/CD8 ratio	<.75 (36.9%)	IgG	>1600 (26.0%)
	>400 (14.3%) p=.0001		>.75 (11.1%) p=.0001		<1600 (14.2%) p=.003
IgA	>250 (37.3%)	C1q binding	>8% (30.5%)	Hbg	<15.0 (28.4%)
	<250 (9.3%) p=.003		<8% (6.1%) p=.034		>15.0 (7.2%) p=.029

Cox regression revealed that CD4 cell depletion, IgG elevation, and IgA elevation, were *significant and independent* predictors of progression to AIDS in seropositive homosexual men.

Of 345 men who were HIV negative at enrolment, 85 (25%) have seroconverted by the time of this analysis. The K-M estimate for the risk of seroconverting during 11/82-07/86 was 22.5%. The seroconversion rates during 5 successive 9 month periods from 11/82 to 07/86 were 4.4%, 9.1%, 5.2%, 4.3%, and 1.7%. Cox regression analysis revealed the following significant risk factors for seroconversion: *number of sexual partners, receptive anal intercourse, history of gonorrhea, use of illicit drugs, and age below 30 in 11/82.* That men under 30 were twice as likely to seroconvert as older men appears to be due to lesser modification of behavior in the younger group. In fact, the proportions of men in the age groups <30, 30-34, 35-39, and 40+, reporting a decrease in the annual number of sexual partners were 49%, 56%, 61%, and 68% respectively. Additional counselling about safer sexual practices should therefore be selectively directed to younger members of the gay population.

M.3.4 Natural History of HIV Infection in Intravenous Drug Abusers (IVDAs)

PETER A SELWYN*, EE SCHOENBAUM*, D HARTEL*, T PETERMAN**, RS KLEIN*, GH FRIEDLAND*, et al, *Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, **CDC, Atlanta, GA, USA.

We are prospectively studying patients in a methadone maintenance program in NYC to characterize the natural history of HIV infection in this group of IVDAs. From 7/85-4/86, 498 patients enrolled in an HIV seroprevalence study; we now present preliminary follow-up data. All subjects had an initial interview regarding drug use and sexual behavior, serum was obtained for HIV antibody (Ab) and a physicial exam was performed. Rescreening visits are scheduled semi-annually, with interview, repeat Ab test, and exam. All patients receive on-site primary care and are monitored by clinical staff for the occurrence of AIDS/HIV disease.

In the original group, there were 169 seropositives (SP) without AIDS, and 329 seronegatives (SN). 91 (54%) SPs were male; mean age was 33 yrs.; 17 (10%) were white (W), 54 (32%) black (B), 98 (58%) Hispanic (H). 5 of 6 SPs with oral thrush (OT) at study entry developed AIDS at a mean of 4.7 mos. follow-up. 163 SPs without OT have been followed for a median of 15 months (range 10-20). Of these, 6 (3.7%) developed AIDS and 2 (1.2.%) presumptive AIDS at a mean of 12.3 mos. follow-up. Among SPs without OT, cumulative incidence of AIDS was thus ~5%, with 2.7 cases/1000 person-months follow-up. Of 13 cases of AIDS/presumptive AIDS, 8 (62%) were male; mean age 34 yrs.; 1 was W (8%), 6 B (46%), 6 H (46%). Multiple logistic regression analysis including demographic, drug use, and sexual variables from initial interview data indicated that black race ($p<.01$), prostitution ($p<.02$), and drug use in a "shooting gallery" ($p<.03$) were all predictive of the development of AIDS among SPs. 44/169 (26%) original SPs have been formally rescreened to date. 5/44 (11%) had new generalized lymphadenopathy on exam and 2/44 (5%) had new OT at a median of 14 mos. follow-up.

Results indicate that HIV-infected IVDAs progress to clinical disease at a substantial rate; AIDS was predicted by certain drug use and sexual behaviors. The observed association with race requires further explanation.

M.3.5 Risk of Disease in Recipients of Blood from Donors Later Found Infected With Human Immunodeficiency Virus (HIV)

J.W. WARD*, D. DEPPE*, H. PERKINS**, S. KLEINMAN***, P HOLLAND+, J Allen*, *Centers For Disease Control, Atlanta, Ga,** Irwin Memorial Blood Bank, San Francisco,*** American Red Cross, Los Angeles, + Sacramento Blood Center, Sacramento CA.

Recipients of blood from donors later found infected with HIV are unique in that their date of infection is known, and the natural history of HIV infection may be more easily observed. We have identified 777 recipients of blood from 131 donors later found to be infected with HIV. Of 457 recipients investigated, 155 (34%) survived less than 4 months post-transfusion, 249 (54%) survived longer than 4 months, and 53 (12%) were lost to follow-up. Of those who survived longer than 4 months, 18 (7%) developed AIDS 10 to 63 months after transfusion (median 28 months). Of the 54 HIV-seropositive recipients followed an average of 46 months after transfusion, 28 (52%) have remained asymptomatic, 12 (22%) have generalized lymphadenopathy, 9 (17%) have AIDS-related complex, and 5 (9%) have developed AIDS. Of these 54 recipients, 13 (24%) had an acute illness compstible with acute retroviral syndrome. Of 19 tested asymptomatic seropositive recipients, 14 (74%) had low T-cell helper:suppressor ratios. The 49 seropositive recipients without AIDS were not significantly different than the 18 who developed AIDS by sex (47% male vs 39% male), age at transfusion (49 years vs 52 years), and total blood received (7 units vs 16 units). However, the 18 AIDS patients more frequently had blood and clotting disorders (usually autoimmune) than did the other seropositive recipients (28% vs 0%, $p<0.001$). Blood recipients from infected donors are at high risk for HIV-related disease. The association of blood and clotting disorders with the development of AIDS is under investigation.

M.3.6 Continuing Studies on the Natural History of HIV Infection in Zaire.

BOSENGE NGALY*, R.W. RYDER**, B. KAPITA*, H. FRANCIS***, T. QUINN***, J.M. MANN** et al., *Mama Yemo Hospital and Department of Public Health, Kinshasa, Zaire, **CDC, Atlanta, *** NIH, Bethesda.

In November, 1986 2020 hospital staff members at Mama Yemo Hospital were re-examined for HIV antibodies. Among the 44 employees who were asymptomatically HIV-infected in 1984 and who were followed up in 1986, 2 had developed AIDS (2.3 cases/person years of observation [PYO]). During the 2-year period, an additional 18 of these 44 patients but only 1 of the 1958 persistently HIV(-) patients developed signs/symptoms consistent with AIDS-related complex [ARC] (ARC rate of 20.4 cases/100 PYO in seropositives, .05 rate in seronegatives). Nine of 18 HIV(+) symptomatic patients in 1984 had a marked decline in clinical status when re-seen in 1986. Ten (7.1%) of the 140 1984 HIV(+) employees on whom information could be obtained in 1986 had died.

There were 41 seroconversions during this period for an infection rate of 1.0/100 PYO. Fifty-eight percent of the new infections were in men. The average age of patients with new infections was 41.4 years for males and 35.5 years for females. Twenty four percent of new female infections had had a spontaneous abortion compared with 4% of previously infected and 1% of non-infected women. Nine new infections had ARC at the time they were examined. New infections did not cluster in employee groups having the most contact with patients or their body fluids.

In this representative urban, middle-class, African population with 1% yearly HIV incidence, an important rate of disease progression has been documented.

Virology—Structure and Function I

M.4.1 Pathogenesis of HIV Infection - Virus: Host Interactions

JAY A. LEVY, Department of Medicine and Cancer Research Institute, University of California, School of Medicine, San Francisco, CA, 94143.

The human immunodeficiency virus (HIV) is a human lentivirus that has a variety of heterogeneous subtypes. They can be distinguished by replicating properties in different cell types, cytopathology, induction of a latent state, sensitivity to serum neutralization, restriction enzyme patterns, and nucelotide sequences, particularly in the envelope region. These properties of HIV contribute to the pathogenicity of some isolates. The immunologic responses of the host determine whether the infection with HIV progresses to disease, or whether the virus is kept under control. Strong cell-mediated immune responses appear responsible for suppression of virus replication and spread. Other immune reactions may advance the state of the disease, such as autoantibodies against platelets, helper T lymphocytes and other host cells. The formation of immune complexes containing HIV antigens and viral proteins may compromise immune function. The malignancies in AIDS may result from an enhanced response of certain cells in the immune system. B cell lymphomas may result from lymphokine or antiidiotype production, and Kaposi's sarcoma may represent proliferation of endothelial cells responding to enhanced angiogenesis-promoting factors. These malignancies may be linked as well to Epstein-Barr virus, CMV or papova viruses. The pathogenesis of HIV infection, therefore, is the end result of an interplay between particular HIV with specific host responses. An understanding of the factors involved is important in our approaches at control and prevention of HIV infection.

M.4.2 Clonal Analysis of Functional Differences of Human Immunodeficiency Virus (HIV)

SHINJI HARADA*, N. YAMAMOTO**, Y. HINUMA*, Institute for Virus Research, Kyoto University, Kyoto 606, **Dept. of Virology and Parasitology, Yamaguchi University, School of Medicine, Yamaguchi, 755 Japan.

Different isolates (HTLV-IIIB, LAV-1, ARV-2) of HIV were cloned by a novel plaque-forming method using a HTLV-I carrying cell line MT-4. All viral preparations were titrated by reverse transcriptase (RT) activity and plaque-forming unit (PFU). PFU/RT values which indicate the relative proportion of incomplete and infectious viruses were used for the determination of the viral infectivity. High values were obtained mainly from clones of HTLV-IIIB and LAV-1, while low values were from ARV-2-derived clones, suggesting that ARV-2 and its clones were genetically less infective. To assess cytocidal effect of the viruses, we selected and used 4 clones with similar PFU/RT value (infectivity) for proliferation assay of infected MT-4 cells, one (HTLV-IIIB-C-2) of which was found to kill more cells than others even at the same doses (MOIs). Furthermore, plaques induced by the HTLV-IIIB-C-2-infected cell were larger than others, suggesting that release (proliferation) of the progeny was maximum in HTLV-IIIB-C-2-infected cell. Among clones tested, three were found to induce strong cytopathic changes (fusion and ballooning) selectively to MT-4 cells. Thus, we concluded that infectivity, proliferation and cytopathic fusion-effect might be encoded by the viral genome and be separable by the plaque-cloning method.

M.4.3 T4 Glycoprotein and T4 Messenger RNA in Human Immunodeficiency Virus-Permissive cells

M. MALKOVSKÝ, KAREN PHILPOTT*, A. MELLOR*, P.J. MADDON**, R. AXEL***, A.G. DALGLEISH, et al., Retrovirus Research Group and *Transplantation Biology Section, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England; **Department of Biochemistry and Molecular Biophysics and ***Howard Hughes Medical Institute, College of Physicians and Surgeons, Columbia University, New York, New York 10032, USA.

The mere presence of the T4 molecule on the surface of both human lymphoid and non-lymphoid cells is sufficient to render the cells ausceptible to human immunodeficiency virus (HIV) infection in vitro (Maddon et al., Cell 47, 333-348, 1986). Recently, we have identified a B-lymphoblastoid cell line (Cupta) which expresses neither T4 on the cell surface (FACS analysis) nor T4 mRNA (Northern blotting, S1 nuclease protection assay). However, Gupta cells can be productively infected with HIV using a relatively low dose (10 infectious units per ml) of virus. Interestingly, the HIV infection of Cupta cells is not associated with syncytial formation, which is typically induced by HIV in T4-positive cell lines. Also, the CD4 monoclonal antibodies (anti-Leu-3a and DAKO-T4), which block the cytopathic effect of HIV on T lymphocytes do not inhibit the HIV infection of Cupta cells. Finally, we have studied several monkey species and found that T lymphocytes of the olive baboon (Papio anubis) and the common marmoset (Callithrix jacchus) express certain epitopes pertinent to HIV infection, suggesting that these species could serve as a model of HIV infection in vivo.

M.4.4 Delineation of a Region of the HIV gP12D Envelope Protein which Interacts with the CD4 Antigen of the Helper T Lymphocyte

LAURENCE A. LASKY, T. GREGORY, G. NAKAMURA, C. FENNIE, D. SMITH, P. BERMAN, et al., Departments of Molecular Biology, Process Development, and Assay Development, Genentech, Inc., So. San Francisco, CA, USA.

The most important initial event in the infection of cells by HIV is the interaction between the virus envelope protein, gP120, and its cellular receptor, the CD4 antigen. In order to understand this interaction, we have begun to investigate the regions of the envelope antigen which interact with the CD4 protein. Previously, we demonstrated that large quantities of a secreted form of the HIV gP120 antigen could be produced in permanent mammalian cell lines. A radiolabelled form of this envelope protein has been found to bind to a recombinant CD4 antigen with high affinity, and this binding can be inhibited by the appropriate OKT4 monoclonal antibodies as well as human neutralizing sera. A number of monoclonal antibodies specific for gP120 have been tested for their ability to block this interaction, and one has been found to be effective. The gP120 epitope which interacts with this blocking monoclonal antibody has been isolated by passing a mild acid hydrolysate of gP120 over an immunoaffinity column which utilized the blocking monoclonal antibody. One peptide specifically bound to the column, and N-terminal sequencing revealed that it was located in the C-terminal portion of the envelope protein. In order to further analyze this region, in vitro mutagenesis of the HIV envelope gene was used to delete a small region of the envelope protein within the peptide which bound to the blocking monoclonal antibody. The resultant mutant gP120 protein was unable to bind to the CD4 antigen.

M.4.5 Reversion of a Non-infectious Envelope Mutant of the Human Immunodeficiency Virus in a Tissue Culture System.

RONALD L. WILLEY*, DANIEL J. CAPON**, THEODORE THEODORE*, MALCOLM A. MARTIN*. * Laboratory of Molecular Microbiology, NIAID, NIH, Bethesda, MD 20892; and **Genentech, Inc., South San Francisco, CA.

Site specific mutagenesis has been used to introduce a single amino acid substitution within the env gene of the human immunodeficiency virus (HIV). The substitution of a glutamine for an asparagine codon at a potential N-linked glycosylation site within a highly conserved region of env gp120 resulted in the production of defective virions. Particles produced following transfection of the mutant clone into a colon carcinoma cell line were unable to infect $T4^+$ lymphocytes. However, revertant infectious particles appeared in long-term cocultures of transfected colon cells and $T4^+$ lymphocytes. In three of nine experiments, infectious virions were detected at 26, 35, and 38 days after the addition of lymphocytes. Revertant proviral DNAs were cloned and their env genes sequenced. These results indicate that the HIV genome can undergo variation during replication in tissue culture in the absence of any immune pressure.

M.4.6 Structure/Function Relationships of the HIV Envelope Glycoproteins

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The HIV envelope glycoproteins play a central role in virus entry into the host cell and in the direct cytopathic effect of HIV infection on T4 bearing cells. Plasmids expressing mutant HIV envelope proteins were constructed and used to transfect human T and B lymphocyte lines. Expression and processing of the HIV envelope was monitored as well as the ability of the mutant envelope protein to bind to the T4 receptor and to induce the formation of syncytia by membrane fusion. Mutations affecting the association of the gp120 exterior protein and the gp41 transmembrane protein, mutations affecting the binding of the gp120 to the T4 molecule, and mutations affecting post-T4-binding steps in the process of syncytium formation were defined. The ability of anti-peptide sera or sera from HIV infected individuals to interfere with the function of envelope proteins derived from divergent HIV strains was examined.

Psychosocial—Behavioral Studies of AIDS

M.5.1 Neuropeptides and the HIV receptor: Peptide T_{4-8} and its Pentapeptide Analogues are Potent CD_4 Receptor Ligands Present in env of All HIV Isolates.

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We have previously reported on the deduction of peptide T as the putative attachment sequence by which HIV binds to macrophages, T cells, and brain cells (Pert et al PNAS 83,'86). We have obtained [^{3}H]-D-Ala$_1$-peptide T and developed specific receptor binding assays to the 60 kD T_4 molecule present on rat, human, and monkey brain membranes as well as human T cells and mouse macrophages. The core sequence necessary for CD_4 receptor activity is the pentapeptide TTNYT whose analogues appear in all HIV isolates obtained to date as well as HTLV I and II. Pentapeptides have been synthesized and demonstrated to have potent bioactivity in human monocyte chemotaxis (Ruff et al FEBS 211), and in displacement of [^{3}H] peptide T from human T cells, rat hippocampal membranes, and mouse macrophage membranes. T_4 receptor binding can be detected only on T_4 positive clones, but not on T_4 negative clones. D-amino acid Tyr substitution in the critical, highly conserved 4 position results in a virtual total loss of bioactivity. Requirements for tertiary structure for bioactivity will be described. The original anti-viral demonstration has been extended to A3.01 cells in which 10^{-10} to 10^{-8}M peptide T and its pentapeptide analogs reduce infectivity of the entire course of infection by 80-90%. VIP, a neuropeptide enriched in cortex and sacral autonomic ganglia, shares structural homology since VIP7-11 is TDNYT and this neuropeptide is active at CD_4. We hypothesize that the VIP-mimetic properties of HIV env produce the profound immunological failure and psychotomimetic disorders chracteristic of AIDS.

M.5.2 Carl Eisdorfer, University of Miami, Miami, Florida.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

M.5.3 PSYCHOIMMUNOLOGIC RESEARCH AND AIDS

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The neurotrophic nature of HIV infection has led to numerous clinical descriptions of CNS correlates of AIDS, ARC, and HIV infection. These include cognitive, motor, and behavioral change believed secondary to HIV infection itself rather than to the opportunistic CNS infections consequent to the profound immunologic dysregulation of AIDS. AIDS treatments are proposed or being tested that are known to be associated with demonstrable neuropsychiatric sequelae. Not only the neurotrophic nature of HIV, but also the increasing documentation of the interdigitation of the immune, endocrine, and central nervous systems predict that an immunologic infection by HIV would have CNS consequences and that effective treatments will either be active in the CNS and/or have side effects in the CNS. Data will be reviewed addressing the biobehavioral basis for AIDS research arising from the integration of the immune and central nervous systems. Evidence for the identity of neurotransmitters and immunotransmitters will be presented as well as emerging research on the impact of behavior on immuno/neurotransmitters and the behavioral sequelae of immuno/ neurotransmitter modulation. This paper serves both to provide background for the other papers presented in this session as well as to discuss a future direction of AIDS research in the near term.

M.5.4 An unspeakable Disease.Self-Isolation of HIV infected pa= tients as a result of Conflicting Aspirations

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104 patients (38 AIDS,14 ARC, 43 Lymphaden.,9 Asympt.)of a Paris hospital were interviewed in March and April 1986 about changes in their social and work relationships, psychological stress and their speaking about the diagnosis. Most patients including married men and gays living in couple relationships speak only with the closest persons, 50% of L and A and 30% of ARC and AIDS with nobody about their illness.Except for a drastic decline in sexual activities, nothing apparently changes in their personal life and work before longer periods of hospitalisation.Although suffering from insomnia, depression and anxieties, only 6% of patients sollicit or accept psychological and psychiatric help, less than 10% support services offered by associations. Patients tend to refuse help becouse con= tinuing a "normal life" symbolizes hope. But this is only possible by hiding ones diagnosis.This attitude then hinders mobilizing sup= port around them.This suggests that patients live with contradicto= ry aspirations that compare to a double bind situation as seeking help and breaking the silence is easily identified with giving up one's hope and abandoning one'self in a situation overdetermined by the threat of death.

Only wide social acceptance of HIV infection as a "normal diseaee" can help to solve this psychological dilemma.

M.5.5 **An Intensive Psychoimmunologic Study of Long-Surviving Persons with AIDS**

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Given the increasing number of studies which link stress and/or behavioral factors with immune response and disease progression, psychosocial factors might be expected to play a role in AIDS. While there has been much interest and speculation about the relationship of psychologic and immunologic factors in AIDS, there are no completed studies in this area, to date. The present study is concerned with the interactions among psychosocial, immunologic, and psychophysiologic parameters in persons with AIDS who have varying durations of survival.

Initially, 5 subjects were diagnosed with AIDS for less than one year ($\bar{x}$= 8 months), 8 were diagnosed between 1 and 2 years ago ($\bar{x}$= 19.9 months), and 5 "long-surviving" men were diagnosed more than 3 years ago ($\bar{x}$= 42.4 months). Blood was drawn prior to an initial psychosocial interview and 6 weekly interviews addressing recent emotional experiences and related coping patterns. Blood was assayed for helper-inducer and suppressor-cytotoxic T cell numbers and ratio, Natural Killer cell numbers and function, virus "specific" T cells, large granular lymphocytes, activated suppressor cells, activated helper cells, B cells, and cortisol levels. The six emotion-related interviews were videotaped and subjects were monitored for heart rate, skin temperature, skin conductance, and respiration. Various psychosocial measures were administered to assess social support, stress, daily moods, health-promoting activities, and psychological "hardiness." Relationships among immunologic and cortisol levels, psychophysiological reactivity, emotional expressiveness, and stress/coping indices will be presented. The data analyses focus on within subject patterns of co-variation, as well as differences across subjects, particularly, patterns that distinguish "long-surviving" persons with AIDS. Further analyses will investigate factors related to actual duration of survival from time of diagnosis.

M.5.6 **Viral lipids as a site of action for developing novel anti-viral agents: Studies with AL721.** A. S. Lippa[1], F. T. Craws[2], M. H. Grieco[3], E. Bulmovicl-Klein[3], M. Lange[3], D. I. Scheer[4], and C. A. Klepnar[1]; [1]Praxis Pharmaceuticals Inc., Beverly Hills, CA., [2]University of Florida Medical School, Gainesville, FLA, [3]St. Luke's/Roosevelt Hospital Center, New York, NY, [4]Yale University School of Medicine, New Haven, CT.

A major underlying theme in biology is the understanding that many important processes involve the recognition of biologically relevant substances by specific receptor molecules. This theme can be observed in such diverse processes as 1)the attachment of neurotransmitters to their appropriate receptor protains, 2) the binding of antigens to antibodies and 3) the infection of host cells by viruses. In these cases, successful receptor binding is highly dependent on the orientation and tertiary conformation of the interacting molecules, which in the case of membrane proteins is regulated by the lipid composition of the membrane. Human immunodeficiency virus (HIV), an enveloped retrovirus, attaches to T4 lymphocyte receptors with high specificity. Based on the high lipid composition (approx. 50%) of HIV, its hyperviscous nature and abnormally high (≥1) cholesterol to phospholipid molar ratio (C/P), we believe that the viral envelope may have an important role in maintaining the structural integrity and infectivity of the virus by providing a rigid lipid matrix enabling the viral attachment proteins to maintain the proper conformation/orientation for binding to T4 receptors. AL721 is a unique mixture of orally active lipids which has been shown previously to modify membrane lipid composition and to enhance lipid bilayer membrane fluidity by the extraction of cholesterol from cell membranes with high C/P. Treatment with AL721 decreased the cholesterol content and altered the biophysical properties of HIV envelope in parallel with its ability to inhibit the infectivity of HIV. In eight patients presenting with persistent generalized lymphadenopathy and who were seropositive for antibody and virus, eight weeks treatment with AL721 decreased mean blood levels of reverse transcriptase activity by 60% and increased the diminished lymphoproliferative responses to both pokeweed and concanvalin A mitogens. These data support the hypothesis that the HIV membrane is a major structural component of the virus and that modifications in viral lipid composition by AL721 may prevent viral infection of host cells.

Prevention/Public Health—Impact of HIV Testing on the Behavior of Homosexual Males

M.6.1 Effect of HIVab Serodiagnosis on Sexual Behavior in Homosexual Men in The Netherlands

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Between October 1984 and October 1986, 860 homosexual men, living in and around Amsterdam, The Netherlands, were surveyed every six months, regarding sexual behavior. At the start of the study 746 subjects learned their HIVab status, of whom 234 (31 per cent) were HIVab+ . In addition 114 individuals, recruited as controls, were not tested on HIVab. Regarding changes in sexual behavior, data were analysed with analysis of variance in a doubly multivariate repeated measures design. To improve the comparability between groups (obscured by pretest differences in group means and a differential "floor" effect) deviation scores were computed. These express the relative popularity of each sexual technique in relation to all other techniques.

Reductions were found in the number of sexual partners and the number of partners on all measured sexual techniques. HIVab tested individuals reported greater reductions than did controls. Cases who were HIVab+ reported the greatest reductions. The relative popularity of masturbation active and passive and anogenital insertive and receptive intercourse remained constant. Oro-oral sexual contact and orogenital insertive and receptive intercourse became less popular, while oroanal insertive and receptive intercourse became slightly more popular. No substantial differences between groups were found in this respect.

M.6.2 Factors Influencing the Decision to Learn HIV Antibody Results in Gay and Bisexual Men

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During the latter part of 1985, 1809 gay or bisexual men enrolled in the Pittsburgh cohort of MACS (Multicenter AIDS Cohort Study) were invited by mail to learn their HIV antibody results. Participants were asked to complete and return a questionnaire designed to assess the factors influencing their decision about learning results, their recent sexual behavior, their knowledge about AIDS and their attitudes towards AIDS risk reduction. 869 (48%) men accepted the invitation, 160 (9%) declined and 780 (43%) failed to respond. There were no significant differences in demographic, behavioral and attitudinal characteristics or HIV seroprevalence between the men who accepted and those who declined. However, significant demographic differences were noted between the men who responded to the invitation versus those who did not, in that the latter group was comprised of a greater proportion of men who were younger, non-white or less well-educated. The most frequently cited reason (87%) why men wanted their results was to determine if they had been infected with HIV. Of those who declined, 31% cited concerns about the psychologic impact of learning about a positive antibody result as being the most important reason for their decision to decline. The most frequently selected contributing reason for declining results (61%) was the belief that the test is not predictive of the development of AIDS. 24% believed that the test is inaccurate and 19% expressed concerns about confidentiality. These findings have relevance to the design and implementation of HIV screening programs.

M.6.3 Sexual practices and condom use in a cohort of homosexual men: Evidence of differential modification between seropositive and seronegative men.

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We have been following a cohort of approximately 600 homosexual men recruited through 6 general practioners with six-monthly questionnaires, physical exams, and lab testing. To assess behavioral change, we compared sexual practices reported at the earliest visit (EV) during the period [03/84 - 12/84] with those reported at the latest visit (LV) during the period [05/85 - 09/86] in all 430 members of our cohort who had complete data for at least 2 visits during the observation period. This included 150 seropositive men with a mean interval between EV and LV of 19.4 months (range=8-28) and 280 seronegative men with a corresponding mean interval of 20.1 months (range=6-29). Overall, the mean annual number of sex partners declined from 7.7 to 6.4 (p<.001). This was confined primarily to the seropositives (9.2 to 5.8; p<.001), as compared to the seronegatives (6.9 to 6.7; p=NS). Because the seropositives had higher levels at EV and thus greater potential to decline, we restricted the analysis to the upper 50% at EV. In this analysis, the seropositives declined from 16.2 to 7.7 (p<.001) while the seronegatives declined from 15.6 to 10.9 (p<.001), with the decline being significantly greater in the seropositives (-8.5 vs -4.7; p=.043).

To study condom use in high risk situations, we analyzed their use during *receptive* anal intercourse with *casual* partners among those men in the upper 50% of casual sexual contact. At LV, 35% of seronegatives and 7% of seropositives reported *never* using condoms during this activity (p<.001) while only 42% of seronegatives and 44% of seropositives reported *always* using condoms during this activity.

These data suggest that the very people at continuing risk, namely seronegatives, may have modified their behaviur to a lesser degree. Even within an AIDS related study with six monthly visits, less than half of seronegatives reported *always* using condoms during receptive anal intercourse with casual partners as of their most recent visit. The data suggest that we need to redouble our efforts at educating all people at risk regardless of their HIV status.

M.6.4 The HIV Antibody Test: Influence on Sexual Behaviour of Homosexual Men.

CHARLES F FARTHING*, W JESSON**, H-L TAYLOR**, A G LAWRENCE*, B G GAZZARD*. *St Stephens Hospital, London, UK. **Public Health Laboratory, Collindale Laboratories, London, UK.

There has been debate as to whether patients at risk of HIV infection should be encouraged to have an HIV antibody test performed. We therefore conducted a survey by anonymous questionnaire which was completed whether or not the test was eventually carried out. All patients were counselled prior to being offered the test and a similar questionnaire was completed 3 months after the initial interview. Of 324 homosexual men offered the test 87% agreed to be tested although 157 had come to the clinic without this intention. Only 4 patients did not wish to know the results. Sixty five per cent of patients had already modified their sexual behaviour but 93% thought they would be more likely to adhere to safer sexual practices if shown to be positive whereas 79% would do so if the test was negative.

Three months later 16% of patients regretted having the test - all had had a positive result. Half of the 83% of patients practicing safer sex felt they were doing so as a result of the counselling, but the rest as a result of the test being positive.

Our results suggest that the majority of gay men (88%) wish to know their HIV antibody status and that having the test performed encourages the adoption of safer sex practices.

M.6.5 Evaluation of Anti-HIV Testings in Sweden, a Country where HIV Infections are Subjected to Legislation

Professor M. BÖTTIGER M.D., Nat. Bact. Laboratory, Stockholm, Sweden

In Sweden testings for presence of anti-HIV are encouraged. However, all physicians carring out the tests must be able to give psychosocial help and advice both to the afflicted and those who are seronegative but at risk. In November 1985 the HIV infection was included among the veneral diseases subjected to legislation. The number of tests performed and the number of positive test results in this country with 8.3 million inhabitants have been reported since then. Up to 1987 115,000 tests (blood donors excluded) were reported - 10,000 thereof from homosexual men and 13,000 from drug addicts. Persons at risk were as a rule investigated several times.

The number of tests performed did not decrease significantly during the period before and after legislation. However the yearly number of new seropositive persons diagnosed declined from 836 in 1985 to 570 in 1986. The number of seropositive blood donors also successively decreased from 13 in the first 530,000 tested to none of the 200,000 tested the last half of 1986.

HIV-infected persons are reported from the physicians to the central epidemiological department under a code. The same code is used in reports directly from laboratories. The two report systems are in agreement with each other.

M.6.6 Safer Sex and accentance of testing.Results of the nation= wide annual servey among French Gay Men

Michael POLLAK*,M.A.SCHILTZ*,B.LEJEUNE*, *GSPM,CNRS,Paris,France*,GPH, Paris,France.

- An annual nationwide survey among French Gay Men(sample size: 1200) shows considerable changes in sexual behavior between 1985 and 1986. Number of partners has decreased, condom use has increased from 5% to 33%, more than 10% no longer practice anal sex, some 30% never did.At the same time volontary testing is widely accep= ted, as revealed by more than 30% of the respondents already tested in 1986. One out of three tested gay men being HIV-positive. Knowing ones test results does not necessarily translate into safer sex practices. One can rather say that the same factors are con= ducive to both safer sex and testing: - Confidence in medical authorities and past regular STD surveillance; - self confidence and social acceptance of one's homosexuality; - proximity with AIDS victims; - existence of a 'privileged' (although not necessa= rily exclusive) love relationship that provides emotional security.

Roundtable Discussion

M.7

Communicating AIDS Education Across Cultural Barriers

Panel Organized By: Paul Kawata
National AIDS Network
Washington, D.C.

Panel Moderator: Gil Gerald
National AIDS Network
Washington, D.C.

Juan Ramos, National Institute of Mental Health, Rockville, Maryland

Carl Bean, Minority AIDS Council of California, Los Angeles, California

Gloria Rodriguez, NJ State Department of Health, East Orange, New Jersey

William Smith, Academy for Educational Development, Washington, D.C.

Jaime Sepulveda, Colonia Valle, Mexico

Epidemiology—AIDS in Developing Countries

M.8.1 Infection by HIV among populations of six countries of Central Africa.

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From 1985 to 1987, O.C.E.A.C. carried out 25 serological cluster sample surveys in joint authorship with Ministries of Health of the six Member-states of the Organization. More than 9000 randomly selected peoples living in six countries of Central Africa (Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea and Gabon) were concerned.

Rural and urban areas were investigated in different climatic zones. Various group of age were studied. The collected blood samples were first screened by ELISA test, then positive cases were confirmed by Western Blotting.

Circulation of HIV within some of the populations of the Sub-region is confirmed, with seroprevalence rates from 0 to 5 % with Western Blotting.

Heterosexual spread of HIV is the major way of infection. Under the age of 15 seroprevalence rates are significantly ($p = 0.01$) lower than those observed in adults. Each sex is equally concerned.

Urban areas are very significantly more affected than rural areas ($p = 0.001$)

Incidence rates were evaluated by the comparison of the results of several surveys carried on in the same place after intervals of 12 or 24 months.

M.8.2 HIV Antibody Prevalence in Migrant Mineworkers in South Africa during 1986.

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Some 512 000 employees on the Gold and Platinum Mines of South Africa are black male migrant workers recruited from various countries in Southern and Central Africa. They live in male hostels for an average of 12.7 months and return home for an average of 3.3 months. Concern about a rising incidence of sexually transmitted diseases in these employees and reports of a high prevalence of HIV infection in Central Africa prompted this study.

During 1986, 330 000 blood specimens were taken at routine medical examinations from all migrant workers returning to work. A total of 29 961 specimens were systematically selected for HIV antibody testing, yielding unbiased samples, stratified according to country of origin. The fresh sera were screened with Abbott or Wellcozyme EIA tests and positives were confirmed by other EIA's, indirect flourescence and Western Blotting if necessary.

HIV antibody prevalence was: Malawi 119/3165 (3.76%), Botswana 7/2063 (0.34%), Mozambique 2/2152 (0.09%), Lesotho 2/2246 (0.09%), Swaziland 1/1885 (0.05%), South Africa 4/18450 (0.02%). These results confirm that there is a low prevalence of HIV infection in Southern African blacks. Malawian mineworkers have a higher prevalence of HIV infection which is probably contracted in Malawi. There is as yet no evidence for spread of HIV infection in the hostel environment.

M.8.3 Risks for Heterosexual Transmission of HIV in Zimbabwe

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In Zimbabwe, interviews with 275 HIV seropositive patients showed that contact with prostitutes (80%), multiple sexual partners (96%) and a history of sexually transmitted disease (STD) (75%) were the risks identified in 200 men. In women, 18% admitted to multiple sexual partners and 51% had a STD history.

We interviewed 75 married couples in whom the husband was the seropositive index case. In 45 both partners were seropositive (T+); in 30 the husband was seropositive and the wife seronegative (T-). T+ men had more sexual partners and episodes of STD in the past two years than T- men. History of genital ulcer in male partners carried a 3 fold excess risk of seropositivity in the female partner (T+ 71% vs. T- 27% p <.001). Syphyllis, chancroid, or genital Herpes were separately associated with transmission (p <.05).

Multiple sexual partners and STDs are the primary risk factors for HIV infection in Zimbabwe. In 60% of couples HIV transmission had occurred, associated with a history of genital ulceration in men. Identification of seronegative wives of HIV seropositive men presents an opportunity to prevent infection.

M.8.4 Incidence of human immunodeficiency virus (HIV) infection and related disease in a cohort of Nairobi prostitutes

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In Africa HIV is a heterosexual sexually transmitted disease. Although there are many studies reporting the prevalence of HIV infection in Africa, few studies of the incidence of HIV infection and the frequency of development of HIV related illness in Africa are available. We began a study of the epidemiology of STD in a cohort of Nairobi prostitutes in January 1985. Initially 65 % of 535 women enrolled were seropositive for HIV. All women were asymptomatic. This cohort has now been followed prospectively for two years for the development of new HIV infections and illness related to HIV. Among initially seropositive women persistent generalizd lymphadenopathy was found in 47 % one year after enrollment. The one year incidence of more severe illness among 298 women evaluated was 5.7 %. These included herpeszoster (8), severe vaginal candidiasis (3), severe weight loss (1), undiagnosed pneumonia (1) and death (3). Among women who were initially seronegative for HIV the incidence of new HIV infection was 56 %. HIV infection is epidemic among this group of Nairobi prostitutes. Illness associated with HIV is developing at rates similar to those observed in European and North American groups. Urgent measures to control this epidemic are required.

M.8.5 The Association between HIV Seropositivity, Blood Transfusions, and Malaria in a Pediatric Population in Kinshasa, Zaire.

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To investigate the role of blood transfusions in the transmission of HIV among African children, we studied 1046 pediatric patients presenting to Mama Yemo Hospital (MYH) in Kinshasa, Zaire. Overall, 147 (14.1%) had histories of previous transfusion, and 40 (3.8%) were HIV seropositive; there was a strong, dose-response association between transfusions and HIV seropositivity ($p<10^{-6}$). To study the clinical indications for blood transfusions, we reviewed 1000 MYH Emergency Ward records and found that 332/480 (69.2%) of the children receiving transfusions had malaria, and 97.3% of all transfusions were given to patients with pre-transfusion hematocrits of 25% or less. We then surveyed 167 hospitalized children and found that 21 (12.6%) were HIV seropositive, 78 (46.7%) had received transfusions during the current hospitalization, and 112 (67.1%) had malaria. Ten of the 11 HIV seropositive malaria patients had received transfusions during the current hospitalization, and four of these children were documented to have been seronegative prior to transfusion. The treatment of malaria with blood transfusions is an important factor in the exposure of Kinshasa children to HIV infection.

M.8.6 Pattern of HIV Infection in Haiti: 1977-1986

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The prevalence of antibody to HIV (wv, p24, gp120) was determined in 2464 Haitians evaluated in Port-au-Prince in 1985-1986 and in 191 Haitians bled during a 1977-79 dengue outbreak. Among AIDS contacts, seroprevalence was highest among heterosexual sex partners (N=174, 55%). Rates in their siblings and friends were higher in males (N=168, 22%) than in females (N=76, 9%). Among unrelated groups, the seroprevalence was 6% for 329 healthy urban adults - 9% in 129 mothers of sick infants, 6% in 109 hotel and factory workers, and 0 in 91 persons of higher socioeconomic status. The rate was 3% in 130 healthy rural adults including 97 mothers of sick infants. Rates among urban tbc pts. (37%) were higher than among rural pts. (15%). 8% of 1037 individuals who had blood tests performed in 3 commercial labs were seropositive. None of the dengue pts. bled in 1977-79 were seropositive. This pattern suggests that HIV is of recent date in Haiti, and is more prevalent in urban areas and in lower socioeconomic groups.

Groups	No. tested	% Seropositive
AIDS patients	384	85
AIDS pts.' spouses	174	55
AIDS pts.' sibs. and friends	244	18
Healthy urban adults	329	6
Laboratory specimens	1037	8
Healthy rural adults	130	3
Tuberculosis patients	166	22
Dengue patients	191	0

Virology—Structure and Function II

M.9.1 T-CELL ACTIVATION INCREASES GENE EXPRESSION DIRECTED BY THE HIV LTR: IMPLICATIONS FOR PATHOGENESIS IN AIDS

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The human immunodeficiency virus (HIV), a lymphocytopathic retrovirus, is the causative agent of the acquired immunodeficiency syndrome (AIDS). In tissue culture systems with T4 lymphoid cells, the amount of HIV replication is related to the extent of T-cell activation. We have utilized transient expression assays in the Jurkat T-cell line to investigate the effects of T-cell activation signals on gene expression directed by the HIV long terminal repeat (LTR). Promoter activity of the HIV LTR was about 10-fold greater in activated T-cells (treated with lectin) than in unstimulated cells. These activation signals are specific for the HIV LTR since expression directed by the HTLV-I LTR, RSV LTR, and HSV thymidine kinase promoter is not affected. The region encompassing the HIV enhancer appears to be the target of T-cell activation signals. The kinetics of induction of expression directed by the HIV LTR closely parallel those for the Il-2 and Il-2 receptor genes. The affects of of T-cell activation signals and the HIV coded transactivator (TAT) gene were observed to be multiplicative. By acting on the HIV LTR, T-cell activation signals may convert a latent infection to a productive infection; thus, T-cell activation may be significant with respect to the onset of clinical AIDS in individuals infected with HIV.

M.9.2 Mapping of the cis-acting Regulatory Regions Responsive to the HIV art gene product.

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The product of the HIV art gene is required in trans for the expression of virion capsid and envelope proteins. However, the block in expression of virus encoded protein in virus defective for the art gene is not absoulute as such mutants can produce a functional tat gene protein. To explain the observed regulatory effects it would suffice for the repressive sequences to be within the env gene as all of the mRNA species that encode virion gag and env protein contain these sequences whereas the mRNA for the tat and art genes does not. To test this hypothesis we designed a novel transient gene expression assay to identify the cis-acting determinants necessary for regulation of gene expression by the art protein. Our results demonstrate that sequences that confer repression of gene expression are dispursed throughout the genome and that these sequences are distinct from those sequences responsive to the art product. One art responsive element, designated ARE, is present within a 40 base pair sequence that contain a highly purine-rich stretch. We propose that the function of art is to relieve repression of gene expression that results from the presence of intragenic repressor sequences.

M.9.3 Human Immunodeficiency Virus Protease

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As for other retroviruses the gag and gag-pol polyproteins of human immunodeficiency virus (HIV) are processed during virus maturation by the viral coded protease which together with RT and endonuclease is translated in a -1 frame relative to the open reading frame of the gag gene. We have analyzed the primary structure of the proteins of human T-lymphotropic virus type-III (HTLV-III) grown in H-9 cells. Proteins were purified from sucrose density gradient banded virus by reversed phase liquid chromatography. Comparison of the determined N- and C-terminal sequences with published nucleotide sequences of proviral DNA identified the proteolytic cleavage products and their order in the $Pr55^{gag}$ and $Pr170^{gag\text{-}pol}$ polyproteins. As expected the amino acid sequences around the maturation cleavage sites were found to show substantial homology.

A peptide corresponding to the C-terminal sequence of HTLV-III protease was synthesized. Antibody to this peptide is now being utilized to isolate the protease in quantities sufficient for further structural and enzymological studies. HIV protease shows sequence homology to other well characterized retroviral proteases which have been shown to have an important role in virus replication and infectivity. Retroviral proteases have conserved in their sequence one of the active-site sequences of aspartylproteases and can be inhibited by certain active-site-directed inhibitors of these enzymes. (Research sponsored by National Cancer Institute, DHHS, under contract No. NO1-CO-23909 with Bionetics Research Inc.).

M.9.4 Functional Analysis of the HIV A (SOR) Gene Product

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We investigated the biological function of the HIV A-gene product by using a mutant of an infectious clone containing a 620 bp deletion in the A gene region (pΔA). When the infectious molecular clone of HIV and the ΔA mutant were separately transfected into the SW480 colon carcinoma cell line, the production of virus particles (as monitored by RT) was readily detected, but a cell-free lysate, containing ΔA progeny virus, could not be passaged into $T4^+$ lymphocytes. In contrast, the ΔA HIV infection could be transferred to $T4^+$ lymphocytes by cocultivation. To ascertain whether the A gene product could function in trans, cDNA clones expressing the A protein were cotransfected with the ΔA mutant and the resulting filtrates were evaluated for their infectivity in $T4^+$ lymphocytes. In all cases examined, the ΔA mutant could be complemented with constructions expressing the A gene; however, the progeny virus from these cultures could not be repassaged in $T4^+$ lymphocytes. These observations suggest that deletion of the A-gene results in the production of particles that are apparently defective at an early step during their replication.

M.9.5 The role of the sor gene of HTLV-III/HIV

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The role of the sor gene of HTLV-III/HIV and its product is not known although initial reports have indicated that it, like 3'orf is dispensible for replication (Sodroski, 1986). To investigate this issue we constructed a series of variants of HTLV-III in which either the entire coding sequences of sor had been removed or termination codons had been introduced into the sor reading frame by site directed mutagenesis. These mutants were capable of generating virus particles upon upon transfection. However, all the mutant clones were extremely limited in their capaciy to establish stable infection in vitro ; less than 1% of cells consistently expressed HTLV-III antigen in cultures infected with sor mutant viruses as opposed to 80-90% of cells in controls (all cultures were monitored for 8-12 weeks). Analysis of cos-1 cells transiently transfected with the mutated clones showed no change in either the quantity or quality of viral RNA, protein or particle expression. Furthermore the ability of these clones to trans-activate remained unaltered when tested in lymhoid and in nonlymphoid cells. These data argue that (i) the sor gene has an important biological role modulating virus propagation and (ii) that this gene most likely acts at a post translational level.

M.9.6 Direct Mutagenesis Analysis of the Trans-Activator Genes of Human T Cell Lymphotropic Virus Type III

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Human T-lymphotropic virus is unique in containing multiple non-structural genes that are regulatory in function. Two of these (tat-III and trs) have been shown to be essential for virus replication based on deletion mutant studies. However, independent roles of these genes in regulation of virus replication have not been elucidated previously. In this study, we used the approach of site directed mutagenesis to generate point mutations in desired nucleotide positions. We obtaind a panel of tat and trs mutants and evaluated their functions by the following parameters: transcription, steady-state mRNA levels, protein synthesis and virus production. The following conclusions could be drawn: 1) Tat-III has a positive trans-acting role in both transcriptional and post-transcriptional events. 2) A chain terminating mutation in the trs gene rendered the provirus defective resulting in a grossly modified viral splicing pattern and unusually high levels of the viral 1.8 Kb mRNA species. Therefore, trs gene product may have a negative trans-acting role in regulating the level of the 1.8 Kb mRNA species. 3) Point mutant proviruses defective in tat or trs were complemented by a wild type tat and trs cDNA subclone allowing the mutants to resume the normal transcription pattern and subsequent virus production. 4) Both tat and trs function in a co-operative manner regulating the virus replication, i.e.; both gene products are required for optimal trancription and translation of the viral structural genes.

Immunology—Viral Proteins and Virus Specific Immune Responses

M.10.1 Analysis with recombinant vaccinia viruses of CD4/HIV gp interaction within individual cells.

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Interaction between HIV gp and CD4 occurs during virus-cell contact (tropism),during cell-cell fusion (syncitia) and,though less well documented,within individual cells (cell death?).In infected cells,the selective and progressive disappearance of CD4 at the membrane,contrasting with conserved CD4 mRNA levels, and intracytoplasmic CD4/gp complexes have been noted, suggesting their causal relationship with cell death. We further investigated this point by infecting CD4+ lymphocytes with various recombinant vaccinia viruses that contained normal or mutated, partial or complete,env gene. Expression of various membrane markers,and gp detection with MAb, was assessed by cytofluorometry on viable cells.Progressive and complete disappearance of Leu 3a staining associated with a 3 to 10 fold decrease of OKT4 fluorescence intensity correlated with increasing expression of gp, which indicates both reduction in the number of CD4 molecules at the membrane and their complexing with gp. Surprisingly, expression of the "natural" HIV gp 110-41 had no effect, and only uncleaved gp 160 or normal gp 110 directly anchored in the membrane through its linkage to a homologous or heterologous transmembrane protein induced such effect. As after "natural" HIV infection, we could immunoprecipitate intracytoplasmic CD4/gp complexes and showed unchanged CD4 mRNA but no cell fusion. Therefore,during "natural" infection of CD4+ lymphocytes, while few cells express viral antigens, complete CD4 modulation indicates that all cells are finally infected, which directly leads to their death.Our results are relevant to the selection of the proper recombinant for vaccination or immune response analysis, and to understand the CD4/gp complex formation and cell death.

M.10.2 Analysis of HIV Protein Presentation on Infected Cell Surfaces: Evidence for Group, Type, and Host Cell Specificity.
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Development of a successful vaccine against HIV requires the identification of proteins on the virus envelope and cell surfaces involved in the immune recognition process. Antibodies were prepared to purified proteins (core and envelope) from HIV (strain HTLV-IIIB) and analyzed by flow cytometry. Antibodies to glycosylated or deglycosylated forms of gp120 bind to HTLV-IIIB-infected H-9 cells, although those against the deglycosylated gp120 react to a lesser degree. Antibodies to gp41, the transmembrane protein, also recognize small amounts of gp41. A polyvalent, monospecific antiserum to p24, the major core protein, did not detect any epitopes on HTLV-III-infected H-9 cells. These results suggest that epitopes of gp41 and glycosylated and nonglycosylated gp120 are involved in the immune recognition process. Thus, they may be important in evoking protective antibodies, whereas epitopes of p24 may not. We also investigated the reactivity of a sequential series of bleeds from a goat inoculated with HTLV-IIIB gp120 isolated from infected H-9 cells with various isolates (envelope strains) of HIV growing in H-9 cells. Both type- and group-specific antibodies were demonstrated by flow cytometry, with the type-specific reactivity occurring (early bleeds) prior to the detection of group-specific (late bleeds) reactivity. Unexpectedly, these antisera showed a marked reduction in reactivity with HTLV-IIIB grown in Molt-3 cells, another human lymphocyte. This reduced reactivity could not be attributed to a lack of production of viral antigen; but rather may reflect cell-specific processing of gp120. Cell-specific processing of gp120 should be investigated further as it may directly influence the immune recognition of envelope preparations.

M.10.3 Cellular Immune Response to Viral Peptides in Patients Exposed to HIV.
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In order to study anti-HIV cellular as well as humoral reactivity in AIDS patients, we measured the proliferative response of peripheral blood lymphocytes to a purified native gag p24 and four recombinant peptides representing various regions of the env gene. These peptides include Penv3 (gp120 amino terminus), PB1 (gp120 midportion), Penv9 (gp120 carboxy terminus + a portion of gp41) and p121 (gp41 subportion). The patients were characterized by their HIV antibody status and general immunocompetence as reflected by the in vitro response to tetanus toxoid (TT).

P24 elicited in vitro blastogenesis in seropositive TT responders but not in TT non-responders nor seronegative controls. Fifty percent of the patients showed humoral reactivity to p24. All seropositive (Western) patients expressed strong humoral reactivity to Penv9 and p121 in contrast to the weak cellular stimulation to these two peptides. PB1 elicited a variable humoral response and little if any cellular response. In sharp contrast to the very weak humoral stimulation, the most impressive cellular response was to Penv3. This showed good cellular reactivity in TT responders, slightly decreased reactivity in TT non-responders and poor reactivity in controls. The cellular response to Penv3 seems to continue after loss of TT reactivity; whereas, the immune response to the core protein p24 is decreased with loss of TT reactivity. These results suggest that regions of gp120 which are recognized by cellular elements (Penv3) may differ from those that stimulate a humoral response (Penv9).

M.10.4 Cellular immune response and neutrallzing antibodies towards HIV in infected individuals.
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To study the relevance of immune response towards HIV to the progression of the disease we measured neutralizing antibodies and T cell responses to purified HTLV-III proteins gp120 and p24 as well as to inactivated whole virions in 28 HIV infected individuals. Neutrallzing antibodies, capable of preventing the cytolytic effect of HIV on a sensitive target cell line, ATH-8, were seen in 66% of the cases. The presence of neutralizing activity correlated with western blot confirmed antibodies to gp120, gp41 and p17. In T cell proliferative assays, a few individuals responded to p24, but no response to the whole virions or to gp120 was seen, not even in cases having remained asymptomatic for 3 years. Prevention of the viral replication with 2',3'-dideoxyadenosine did not increase responsiveness. Moreover, in situ hybridisation revealed only a few infected cells (10^{-3}, 10^{-4}), morphologically belonging to the monocyte - dendritic cell lineage. We have shown that the early anergy to soluble recall antigens in HIV infection is due to infection of the above cells, but in the present material even persons showing normal PPD response had HIV specific anergy. The possibility, that man has an inborn tolerance to the T cell epitopes in HIV external envelope, can be disproved only by direct immunization experiments.

M.10.5 Common and Variable Neutralization Antigens of HIV-1 and HIV-2
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We have shown that sera from HIV-1 infected individuals are capable of neutralizing a genetically diverse range of HIV-1 isolates (Nature, 324, 572-575, 1986). Some HIV-I isolates (e.g. ARV-2) are far more sensitive to neutralization than others.

Sera from HIV-2 infected individuals will cross-neutralize some isolates of HIV-1 but the neutralizing titres are significantly lower than those in the sera of HIV-1 infected individuals. HIV-I sera fail to cross-neutralize the LAV-2 isolate of HIV-2. However, this isolate is poorly neutralized by autologous sera, and low-titre cross-neutralization would be missed. The identification of common neutralization antigens between diverse HIV strains is important for vaccine development.

M.10.6 Antibody-dependent cellular cytotoxicity (ADCC)-inducing antibodies against human immunodeficiency virus (HIV).
Kristina Ljunggren*, E-M. Fenyö**, B. Böttiger***, G. Biberfeld*** and M. Jondal*. Departments of Immunology* and Virology** at Karolinska Institute, Department of Immunology*** at National Bacteriological Laboratory. Stockholm, Sweden.

A method to detect antibodies which mediate HIV-specific ADCC was established using HIV infected monocytoid U937 (clone 2) cells as targets. Simultaneously, the ADCC efficiency of the allogeneic effectorcells was tested with rabbit-anti-b2 microglobulin serum against the same U937 cells. It was found that approximately 40% of all anti-HIV positive sera could induce ADCC killing, irrespective of the clinical stage of the donor. Quantitative comparison of ADCC titers of sera from patients with different severity of HIV infection showed that high HIV specific ADCC titers were more common in symptomfree patients (75%) than in AIDS patients (42%). When the T4:T8 lymphocyte ratio was compared to ADCC titers, no correlation was found. Sera from AIDS patients which had lost antibodies to gag(p19,p24) and pol (p55) proteins, but which were still positive for gp160, 120 and 41, could mediate ADCC.
In further studies, the fine specificity of ADCC active antibodies will be defined using target cells infected with recombinant virus expressing part of the envelope antigens. Also, evaluation of the clinical significance of HIV-specific ADCC antibodies will be needed.

Clinical Management—Cancer, Hemophilia and Cardiovascular Disease

M.11.1 The Clinical, Research and Public Health Applications of the Walter Reed Staging Classification of HIV Infection
R REDFIELD WRAIR Wash DC

In 1985, the Walter Reed Staging Classification of HIV infection was proposed. This staging scheme recognizes that HIV infection as an etiologic disease process in which the central pathogenic event resulting in immunodeficiency is the progressive destruction of the T helper cell population. In addition this scheme recognizes that central nervous system disease, complicating neoplasms, thrombocytopenia and severe constitutional symptoms may have pathogenic mechanisms of occurrence secondary to HIV but independent of functional intregity of the T cell system. The purpose of this talk is to describe the proper excecution of this system, and to demonstrate its multiple applications outlined below. Data will be provided demonstrating its usefulness for each.

1) ROUTINE CLINICAL: a) uniformity of clinical evaluation among health care system; b) pathogenic based framework to clinically approach, manage and follow patients; c) prognostic predictor for physician and patient;

2) RESEARCH: a) facilitate an understanding of the natural history of HIV infection; b) facilitate an understanding of the pathogensis and effect on outcome of associated disease processes; c) facilitate an understanding of the immune response to HIV and its biological significance; d) facilitate the evaluation of therapeudic modalities; e) facilitate an understanding of the efficiency of transmission of different modes and stages of infection;

3) PUBLIC HEALTH: a) facilitate accurate survalence of HIV infection and disease; b) facilitate accurate determination of the incidence of infection; c) facilitate early case identification; d) facilitate the implimentation of public health control programs; e) facilitate the evaluation of the effectiveness of public health invention stragities.

M.11.2 Update on AIDS-Associated Non-Hodgkin's Lymphoma (NHL) in San Francisco.

LAWRENCE D. KAPLAN, PA VOLBERDING, DI ABRAMS, Dept of Medicine, San Francisco General Hospital (SFGH), UCSF Cancer Research Institute, SF. CA, USA.

Forty homosexual men with NHL were treated at SFGH 10/82-12'86. Serologic studies performed in 28 patients revealed all 28, including all surviving patients, to be HIV seropositive. Histologic pattern included small noncleaved (52%), large cell (45%) and cutaneous T-cell (2.5%). Patients presented with Stage IV disease (75%), Stage III (15%), Stage II (7.5%), and Stage IE (solitary lung nodule) in 5%. Extranodal sites included bone marrow (10) meninges (7), liver (5), lung (3), stomach (4), epidural (2), soft tissue (2), nasopharynx (1), other GI (3). Thirty-one were treated with aggressive chemotherapy and 2 received primary radiation therapy. Treated patients without a prior AIDS diagnosis (25) had a complete response (CR) rate of 56% and a median survival of 16.5 mos. Those with a prior AIDS diagnosis (10) had a CR=16% and a median survival=2.9 mos (p=0.04 for survival). There was a direct relationship between relative dose intensity and freedom from relapse. Significant dose reductions were required in 8,9 of those with prior AIDS diagnoses, due to severe marrow suppression, opportunistic infection, or both. While aggressive therapy does prolong survival in some patients, those with prior AIDS diagnoses are less likely to tolerate such therapy, to achieve CR, and to remain disease free.

M.11.3 Clinical Course and Epidemiology of Hodgkin's Disease (HD) in Homosexual Men in San Francisco (SF).

LAWRENCE D KAPLAN, DI ABRAMS, PA VOLBERDING, Dept of Medicine, San Francisco General Hospital (SFGH), Cancer Research Institute UCSF, San Francisco, CA, USA.

Thirteen homosexual men with HD have been diagnosed and treated at SFGH between 5'83 and 12'86. All 9 patients tested were HIV seropositive. 9 (70%) had a prior history of generalized lymphadenopathy or thrush and no patient had a prior AIDS diagnosis. Mixed cellularity histology was present in 9 (70%), nodular sclerosis (NSHD) in 3 (23%) and 1 was unclassified. Stage III or IV disease was present in 12 (92%) with bone marrow involvement in 9 (70%). Five (38%) were treated with MOPP and 7 (62%) with MOPP/ABVD. There were 7 (54%) complete responses, and one of these relapsed. PCP developed in 8 (62%), M. avium in 1 (8%). Three patients (30%) remain alive with active disease at 1,5, and 15 mos from diagnosis. Only one (8%) is disease-free at 24 mos. We compared this group to 35 cases of HD in never-married SF males, age 20-49 diagnosed between 1973-1979. 22 (63%) were NSHD and 8 (23%) were MCHD. Twenty-five (70%) had Stage III or IV disease. 21 patients (60%) and 13 (52%) of those with stage III or IV disease have survived disease free >5 yrs.

The incidence of HD in this SF population has not increased during the period 1980-1985 (relative risk =1.2,1985), suggesting a lack of correlation between HIV infection and development of HD. However, our clinical data suggests a marked alteration in the natural history of HD in HIV-infected individuals, and thus, the importance of serologic testing in this group.

M.11.4 HIV Isolation from Hemophiliacs: Immunological and Clinical Studies.

CHARLA ANDREWS, J. Sullivan, D. Brettler, A. Forsberg, F. Brewster, P. Levine. University of Massachusetts Medical Center, Worcester, MA.

As part of a prospective study of human immunodeficiency virus (HIV) infection in hemophiliacs, blood from 72 individuals without AIDS or ARC was cultured for virus. HIV was isolated from 15 out of 66 (23%) hemophiliacs who were seropositive for HIV, and none of 6 seronegative patients. Virus positive hemophiliacs had significantly reduced T-helper cell numbers, T-helper/T-suppressor ratios, pokeweed mitogen (PWM) responsiveness, total platelet count and a higher incidence of thrombocytopenia (<150,000/ul) when compared to virus-negative patients.

MEAN DATA FROM SEROPOSITIVE HEMOPHILIACS

HIV isolation	n	T-helper (cells/ul)	T-helper/ T-suppressor	PWM (cpm)	Platelets (Plt/ul)	<150,000(%) platelet/ul
+	14	398	.603	7448	187,000	7/14 (50%)
-	51	768*	.806#	12910#	236,137*	9/51 (9.8%)*

*p<.001; # p<.05

The seropositive, virus-positive hemophiliacs also presented with more severe clinical findings than virus isolation negative hemophiliacs. One virus-positive hemophiliac developed AIDS during the study. The mean neutralizing antibody titer did not differ significantly between the virus-negative and virus-positive hemophiliacs. HIV was recultured from 5 out of 6 hemophiliacs up to 1 year later; 9 virus-negative hemophiliacs remained negative for HIV when re-cultured. The significant decrease of T-helper cells and the presence of thrombocytopenia in 50% of the virus-positive group may be a reflection of a heavier virus load, and might be an early marker of more unfavorable prognosis.

M.11.5 International Surveillance for HIV Seroconversion in Hemophilia Patients Receiving Heat-treated Factor Concentrate Therapy.

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Scattered reports in 1986 described HIV seroconversions in hemophilia patients receiving heat-treated factor concentrates (HtFC) produced before donated plasma was screened for HIV antibody. In late 1986, 14 regional and national hemophilia treatment centers in 7 countries of Europe and North America and Australia collaborated to characterize their seroconverters and to quantitate the risk associated with unscreened and screened HtFC. Most of the 1300 seronegative patients under periodic serologic surveillance had previously received unheated FC. Of 450 initially seronegative severe hemophilia A patients, three children still seronegative 6 months after the exclusive use of (unscreened) HtFC, seroconverted thereafter (0.7% of hemophilia A; 0.2% of total). The latest seroconversion was in November 1985. All 3 are asymptomatic, but at least 1 has severe T cell abnormalities and at least 1 other was HIV culture-positive. To provide reliable estimates of the risk of HIV seroconversion associated with screened HtFC which was introduced in these centers between August 1985-July 1986, continued collaborative surveillance is underway to accumulate adequate numbers of patient-years of such therapy. To date, no seroconversions have been noted in nearly 400 patient-years of therapy. By May 1987, the aggregate total for the centers will exceed 1500 patient-years, allowing analysis by type of hemophilia and severity level.

M.11.6 Cardiac Pathology and Cardiovascular Cause of Death in Patients Dying with the Acquired Immunodeficiency Syndrome (AIDS)

DAVID W. ANDERSON*, R. VIRMANI*, A. M. MACHER*, T. O'LEARY*, M. ROBINOWITZ*, W.C. ROBERTS**, et al.. *Armed Forces Institute of Pathology, Washington, DC and **Cardiovascular Pathology, NHLBI, NIH, Bethesda, MD.

The presence of cardiac pathology was retrospectively evaluated at necropsy in 82 patients dying with AIDS in the USA between 1981 and 1986. Myocarditis (MYO), defined according to the Dallas criteria as myocardial necrosis surrounded by inflammatory cells, occurred in 40 (50%) cases. Opportunistic myocardial pathogens were seen in only 14 cases (T. gondii-3, H. capsulatum-3, C. neoformans-3, P. carinii-1, Cytomegalovirus-2, and Mycobacteria spp-2). Dilated cardiomyopathy was diagnosed at necropsy in the presence of biventricular dilatation without significant coronary or valvular heart disease and occurred in 7 (9%) patients, all of whom manifested MYO. In contrast, right ventricular dilatation in the absence of biventricular dilatation was found in 14 (17%) cases and was associated with right ventricular hypertrophy ($p<0.05$), pericardial effusion ($p<0.01$) and opportunistic pulmonary infections ($p<0.05$) but not MYO ($p>0.05$). A clinical cardiovascular cause of death was established in 7 (9%) cases and included 6 patients with MYO (refractory ventricular tachycardia-1, dilated cardiomyopathy with congestive failure-4, and sudden death-1).

Epicardial Kaposi's sarcoma occurred in 9 (10%) cases and was generally not clinically significant. However, in one case extensive pericardial and periaortic involvement led to hemopericardium and death from cardiac tamponade.

Conclusion: Myocarditis is a frequent necropsy finding in patients dying with AIDS and may lead to fatal dilated cardiomyopathy in this population.

Roundtable Discussions

M.12

Prevention and Control of AIDS in Developing Countries

Panel Moderators: Kenneth Bart
Agency for International Development
Washington, D.C.

M. Mukunyandela
Tropical Diseases Research Centre
Ndola, Zambia

Donald Forthal, Department of State, Washington, D.C.

Anthony Meyer, Agency for International Development, Washington, D.C.

Bahman Habibi, National Center for Blood Transfusion, Paris, France

T. Stephen Jones, Centers for Disease Control, Atlanta, Georgia

King K. Holmes, Harborview Medical Center, Seattle, Washington

James Shelton, Agency for International Development, Washington, D.C.

M.13

The Status of Screening: Supplementary Tests for HIV Infections

Panel Organized By: Thomas F. Zuck
Food and Drug Administration
Rockville, Maryland

Panel Moderator: Ian Gust
Fairfield Hospital
Melbourne, Australia

Panel Members: Experts from the United Kingdom, Europe, North America and Australia

M.14

AIDS and the Media

Panel Organized By: Terry Beirn
American Foundation for AIDS Research
New York, New York

Susan Freinkel, Wichita Eagle-Beacon, Wichita, Kansas

Herculamo Siqueira, Denison Advertising, Rio De Janeiro, Brazil

Allen Wurtzel, ABC, New York, New York

Ellen Levine, Women's Day Magazine, New York, New York

Diana Kerew, Diana Kerew Productions Inc., Los Angeles, California

J. G. M. Jagwe, Uganda National Committee on Prevention of AIDS, Entebbe, Uganda

Poster Session

MP.1 INHIBITION OF REPLICATION OF HIV BY AVAROL AND AVARONE

W.E.G. MÜLLER*, H.C. SCHRÖDER* and P.S. SARIN#
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The sesquiterpenoid quinone avarone and its hydroquinone avarol, two natural products from the marine sponge Dysidea avara, have been identified as cyostatic agents that preferentially inhibit growth of T cell lymphoma lines (1). In the present study it is shown that these compounds have a dose-dependent inhibitory effect on the replication of HIV in H9 cells in vitro (2). Both compounds show a significant cytoprotective effect on HIV infected H9 cells at concentrations as low as 0.1 µg/ml (0.3 µM). At this concentration, no inhibitory effect is observed in human or murine peripheral blood or spleen lymphocytes (3). Both avarol and avarone block in a dose-dependent manner the expression of the HIV gag proteins p24 and p15 in the infected H9 cells, and block viral replication as judged by approx. 80% inhibition of reverse transcriptase activity. The potential usefulness of these compounds in the treatment of patients with AIDS and ARC is supported by their following properties (3): "T-lymphotropic" cytostatic activity, B-lymphocyte activating property, antimutagenic activity, low toxicity in mice, high therapeutic indices, and penetration of the blood-brain barrier. A clinical trial to determine the potential antiviral effect of avarol in patients with AIDS is in preparation. (1) Müller,W.E.G. et al.(1985) Cancer Res. 45, 4822; (2) Sarin,P.S.,Sun,D., Taguchi,Y. and Müller,W.E.G.(1986) J. Natl. Cancer Inst.,in press; (3)Müller,W.E.G. et al.(1986)Eur.J.Cancer Clin.Oncol. 22,437

MP.2 AIDS Subacute Encephalitis : Identification of HIV Infected Cells

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Human immunodeficiency virus (HIV) RNA and proteins were detected in 5 brain tissues to 12 AIDS patients with subacute encephalitis, using in situ hybridization and immunohistological labeling with monoclonal antibodies against p18, p25, gp41 and gp110. Staining patterns were superposable with the 2 techniques. A massive and diffuse HIV infection, with clusters of HIV infected cells present in almost every tissue block studied, including spinal cord, was correlated with severe demence and was detected in 3 of these 5 HIV infected patients.

The majority of infected cells were mononucleated and bore processes. Using single and double immunohistological procedures, we identified these cells as macrophages Leu M5+, EBM 11+, KB 90+, 9.4+, HLA-DR+, T6-, DRC-. The majority of them had the phenotype of normal resident brain macrophages/microglial cells (Leu M3-, CD4-), others were labeled with markers of circulating macrophages (Leu M3+, CD4+/-), were present in inflammatory infiltrates and microglial nodules, and were associated with a few infected CD3+/CD8- T cells. We could not detect any infected astrocytes or neurons, all infected process bearing cells were labelled with macrophage markers thus it is very unlikely that oligodendrocytes were infected.

MP.3 Effect of Diethylcarbamazine on Feline Leukemia Virus Infected Cats

LYNN W. KITCHEN, Harvard School of Public Health, Boston, MA.

Eight cats (2 sets of littermates) testing positive for feline leukemia virus (FeLV) antigen in peripheral blood leukocytes were entered into prospective trials to evaluate the therapeutic effect of oral diethylcarbamazine citrate (DEC). Twenty-two additional healthy outbred FeLV cats were also treated with DEC. Pre and post treatment serum viral infectivity was determined for 24 treated cats. Fourteen of these 24 treated cats (58%) initially presented with high titers of serum infectious virus by the assay of Fischinger. Serum viral infectivity became undetectable 1 month after initiating treatment in 12 cats, after 90 days in 1 cat, and after 300 days in 1 cat. Nine cats initially testing negative (<1:10 dilution) for antibody to feline oncornavirus associated cell membrane antigen (FOCMA) tested positive after treatment. Average survival was prolonged by 3 months with DEC treatment in 2 FeLV-inoculated cats in comparison to 2 untreated controls. Survival among cats treated without prospective controls was improved in comparison to an historical control study. DEC treatment has prevented lymphopenia (to date, age 9 months) in 2 naturally-infected FeLV kittens; 2 untreated littermates have both developed lymphopenia. Our results may have implications for humans infected with immunosuppressive retroviruses.

MP.4 Anti-HIV Activity of 3'-Substituted-2',3'-Dideoxythymidine Analogues

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In MT-4 cells 3'-azido-2',3'-dideoxythymidine (AzddThd, AZT) inhibits HIV replication at 0.04 µM, that is at a dose 50-fold lower than in ATH8 cells (1-5 µM). No such increased activity was observed for 2',3'-dideoxycytidine and 2',3'-dideoxyadenosine when evaluated in MT-4 cells. Therefore, this cell line was used to determine the structure-activity relationship of newly synthesized 2',3'-dideoxythymidine analogues modified in the 3'-position.

From this study AzddThd, ddThd and its 2',3'-unsaturated derivative ddeThd emerged as the most potent inhibitors of HIV (complete protection at 0.04, 5 and 0.2 µM, respectively) with an almost identical selectivity index. 3'-Fluoro-ddThd effected 10-40 % protection at 0.008 µM but proved extremely toxic. None of the other 3'-halogenated derivatives of ddThd (i.e. 3'-chloro-, 3'-bromo-, 3'-iodo-ddThd) had a significant HIV-inhibitory effect. The 3'-O-mesyl derivative of ddThd effected 50 % protection against HIV at a concentration of 5 µM without any toxicity at 125 µM, whereas other 3'-O-linked substituents (i.e. 3'-methoxy, 3'-ethoxy, 3'-O-carboxymethyl) virtually annihilated the antiretroviral effect of ddThd. Substitution of a thiocyano group at C-3' of ddThd led to a similar protective activity as seen with 3'-O-mesyl-ddThd, but 3'-thiocyano-ddThd proved also cytotoxic. 3'-Ethylthio- and 3'-hydroxyethylthio-ddThd were less active than 3'-thiocyano-ddThd. Our studies thus revealed that any substituent at the C-3' position of ddThd, with the exception of azido, considerably decreased the antiretroviral effect of ddThd, suggesting a critical function of this part of the molecule in its interaction with its target enzyme(s).

MP.5 **Mismatched Double-Stranded RNA (Ampligen) Protects Target Cells from HIV Infection and Reduces the Concentration of 3'-Azido-3'Deoxythymidine (AZT) Required for Virustatic Activity.** WILLIAM M. MITCHELL, DAVID C. MONTEFIORI, W. EDWARD ROBINSON, and WILLIAM A. CARTER, Vanderbilt University, Nashville, Tennessee, and Hahnemann School of Medicine, Philadelphia, Pennsylvania.

The biological response modifier $rI_n \cdot r(C_{12} \cdot U)_n$, generally referred to as mismatched double-stranded (ds) RNA or Ampligen® was able to protect target lymphoblastoid cells in vitro from infection by the human immunodeficiency virus (HIV). Significant protection of the highly HIV-permissive T-cell line C3 is observed with Ampligen in the 10-50 µg/ml concentration range. Similar results are observed at 50 µg/ml in CEM cells. When administered simultaneously with sub-virustatic concentrations of azidothymidine (AZT), protection of target cells from HIV infection is increased. At higher doses of AZT tested, the virustatic activity observed appeared to be in a synergistic virustatic relationship with Ampligen. Moreover, in combination with Ampligen at least a five-fold reduction in AZT concentration can be used in order to obtain equivalent virustatic activities. Thus, combined therapy with Ampligen and AZT can be expected to be more beneficial to ARC or AIDS patients since current AZT regimens of apparent clinical effectiveness are associated with significant toxicities which undermine its therapeutic potential.

MP.6 **Modification of HIV N-Glycosylation by the α-Mannosidase Inhibitor Swainsonine.** DAVID C. MONTEFIORI, W. EDWARD ROBINSON AND WILLIAM M. MITCHELL, Vanderbilt University, School of Medicine, Nashville, Tennessee.

The two envelope glycoproteins (gp41 and gp120) of human immunodeficiency virus (HIV) serve functions obligatory to the pathogenesis of HIV including attachment of virus to target cells and syncytium formation. Swainsonine is an indolizidine alkaloid found in certain legumes and molds and alters protein N-glycosylation through its potent reversible inhibition of α-mannosidase II (Broquist, H., Ann. Rev. Nutr. 5, 391-409, 1985). Our interest has been to investigate the significance of N-glycosylation in HIV pathogenesis using swainsonine and other inhibitors of glycoprotein processing as tools. We have found that swainsonine affects N-glycosylation of HIV glycoproteins without affecting virus yields. The concentrations of swainsonine utilized in these studies (1-10 µg/ml) had no effect on cell division or RNA and protein synthesis. Synthesis of virus in the presence of swainsonine was confirmed by reverse transcriptase activity in culture fluids and by density gradient centrifugation of [^{35}S] methionine labelled virus. Results of [^{3}H] mannose labelling experiments and SDS-PAGE/fluorography demonstrated that swainsonine causes a reduction in the molecular weight of the HIV envelope gp120 reducing it to a gp110 molecule.

MP.7 **Comparative Study of Human Immunideficiency Virus (HIV) Strains**

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Human immunodeficiency virus (HIV) strains received from France and the U.S.A. and isolated in the U.S.S.R. (including indigenous and imported from Africa) were comparatively studied.

In experiments with monoclonal antibodies a sertain homogenicity of both standard and African strains was shown, and some difference of indigenous strains isolated in the U.S.S.R. was marked.

Restriction analysis showed a more marked variability of the strains studied, although in experiments with molecular hybridization they appeared to be more homogenous. This points to a high frequency of neutral mutations that do not affect amino-acid composition but do affect recognition sites for restriction endonucleases.

Plasmids were obtained that contain non-infectious genome of HIV with removed LTRs and provirus was sequenced. Variations were revealed within all genes, particularly in env region.

A hypothesis is proposed about the existence of a Northern HIV variant with low virulence as compared with American and African viruses. The virus causes predominantely asymptomatic infection.

MP.8 **HIV propogates in human neuroblastoma cells**

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There is evidence that HIV is neurotropic and that its persistence in the CNS is associated with AIDS encephalopathy and dementia in order to characterize HIV persistence in vitro, this laboratory undertook the propogation of HIV in four cell lines, two related and two unrelated to the CNS;it was found that HIV did not propogate in African Green monkey kidney (Vero) cells; human cervix carcinoma (Hela) cells, and human brain astrocytoma cells. However, HIV propogated in a neuroblastoma cell line and attained peak released reverse transcriptase activity 10-14 days post-infection. HIV was also detected using antigen capture Elisa. After prolonged growth in cell culture, there were additional dramatic peaks of released RT activity, 2D-fold greater than the first, and lasting from 36 to 74 days and 110 to 140 days post-infection. The neuroblastoma cell line used is susceptible to HIV and may be useful for HIV replication and isolation studies as well as for a model related to HIV persistence in CNS cells.

MP.9 **Early and late IgM response in HIV infection**

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A total of 463 sequential serum samples from 57 homosexual men, who seroconverted for HIV antibodies (Ab) in IgG ELISA and Western blot assays, were tested by solid phase IgM antibody capture assays. The IgM responses were confirmed by immunoblot, after absorption of IgG Ab, and shown to be predominantly directed to core proteins. Samples were obtained approximately every 3 months and more often in the period following IgG Ab seroconversion. The mean follow-up time was 21 months (10-25 months).

In 30 people no IgM response was found. In 20 people an IgM response, not lasting longer than 3 months, was found approximately concomitant with IgG Ab seroconversion. In 2 people an IgM response occurred 5-9 months after IgG Ab seroconversion and persisted thereafter. In 5 people both a transient early and persisting late (occurring 5-15 months after IgG Ab seroconversion) IgM response were found.

There was no relationship between the presence of "flu-like" disease at HIV-Ab seroconversion and the occurrence of an early IgM response. In 3/7 people with a late IgM response this coincided with expression of HIV antigen (EIA, Abbott Laboratories) and the development of serious HIV related disease. HIV-Ag expression occurred in 5/50 people without a late IgM response and serious disease developed in 2 of those.

MP.10 **Pathologic Features of Cytomegalovirus Retinopathy Following Treatment with the Antiviral Agent Ganciclovir**

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We studied the eyes of 3 AIDS patients with cytomegalovirus (CMV) retinopathy who expired while receiving ganciclovir therapy. Gross, microscopic and ultrastructural studies of these cases revealed varying degrees of retinal scarring and active cytomegalovirus lesions at the margins of the scars. CMV antigens were localized in cells at all layers of retina at the border of the lesions and in isolated cells in a perivascular location within histologically normal appearing retina. These areas probably represent sites of recrudescence when the drug is discontinued. In situ hybridization using a cloned cDNA probe of human CMV corroborated the immunocytologic localization of virus. Ultrastructural studies revealed megalic syncytial cells containing mostly capsids exclusively in the cell nucleus. In situ hybridization using an HIV riboprobe did not detect HIV-infected retinal cells, whereas brain tissue from other cases were positive using the same probe. The cytoplasmic electron-dense membrane bound bodies that have characterized untreated cases of CMV retinopathy were absent in the treated cases. An attempt to isolate CMV in tissue culture from the vitreous and retina of one of the cases yielded a negative result. Our results indicate that ganciclovir does not effectively eliminate CMV from the retina nor does it suppress expression of all viral genes. Ganciclovir appears to function by limiting viral DNA synthesis and subsequent packaging of viral DNA into infectious units, thereby acting as a virostatic chemotherapeutic agent.

MP.11 Human immunodeficiency virus isolates differ in replication potential in vitro.

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Human immunodeficiency virus (HIV) has been isolated from 33 HIV antibody positive individuals with different clinical manifestations of infection. Peripheral blood mononuclear cells (PBMC) from AIDS or pre-AIDS patients yielded virus rapidly as detected by high reverse transcriptase (RT) activity in culture fluids. These viruses were able to establish a persistent infection in several T4 antigen positive tumor cell lines (CEM, H9 and U937 clone 2) and were designated rapid/high. PBMC cultures from individuals with mild or no symptoms yielded virus more slowly and the RT activity was low. Cocultivation of PBMC yielding such slow/low viruses with the T4 positive tumor cell lines showed no or only transient virus replication, as a rule. Cell free transmission of viruses to PBMC from normal donors and to cell lines showed that viruses classified as rapid/high are readily transmitted whereas viruses of the slow/low type replicate poorly, if at all. In fact, slow/low viruses could be divided into 4 groups on the basis of their transmissibility and growth properties. Viruses in group 3 and 4 could efficiently replicate in the Jurkat/tat$_{III}$ cell line allowing radioimmunoprecipitation and restriction enzyme analysis.

MP.12 HIV Entry into CD4+ T Cells Occurs Via pH-Independent Viral Envelope Fusion to the Plasma Membrane

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After binding to specific cell surface receptors, enveloped RNA viruses are known to deliver their genetic information into target cells via at least two distinct mechanisms: (i) by rapid internalization of virus into acidic endosomal vesicles where envelope proteins undergo requisite low pH-dependent conformational changes which facilitate direct virus envelope fusion with endosomal membranes, or (ii) by direct fusion of virus envelope with the plasma membrane of the cell in a pH-independent fashion. CD4 is the cell surface receptor which confers HIV target cell tropism through interaction with mature envelope (gp120); however, the mechanism whereby this enveloped RNA retrovirus enters susceptible cells is not known.

In our studies neutralization of acidic endosomal and lysosomal vesicles (pH > 6.4) with various lysosomotropic agents including chloroquine, NH_4Cl, and monensin, did not prevent HIV entry. Viral entry was quantitated by Slot Blot analysis of cytoplasmic HIV DNA isolated from CD4+ T cells exposed to HIV for 4 hours in either the absence or presence of lysosomotropes. Specificity of the HIV DNA detected was confirmed by Southern blot which revealed a 9.7 kb hybridizable fragment in each treatment group. EM studies of VB cells acutely exposed to HIV at neutral pH revealed direct fusion of virus envelope with the plasma membrane within minutes of mixing uninfected cells with free virus at 4°C. No endocytosed virions were visualized upon rewarming the virus exposed cells to 37°C. These results indicate that HIV preferentially enters CD4+ T cells via pH-independent membrane fusion rather than by a low pH-dependent endocytic route.

MP.13 Characterization of Genetic Mutants of HIV that are Defective in gag Gene Processing.

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An HTLV-III/LAV isolate obtained from an AIDS patient was shown to be poorly infectious for human lymphocytes. SDS-PAGE analysis of proteins associated with this virus, designated HIV(Fre-3), showed that it contained large amounts of the gag viral protein precursor, Pr55. Electron microscopy (EM) of infected HuT 78 cells revealed two populations of virus-producing lymphocytes. One produced virus which matured and had a normal morphogenesis, while the other produced only aberrant "immature" extracellular virus particles. This lymphocyte culture was cloned on sheep choroid plexus cells and 51 single cell clones were obtained. Some of the clones produce infectious HIV (reverse transcriptase positive, mature gag proteins visualized on SDS-PAGE) which by EM appear normal in all stages of maturation. Other single-cell clones release non-infectious, structurally aberrant viruses which contain an electron-lucent core surrounded by a semielectron-dense incomplete ring of ribonucleoprotein, and thus resemble immature extracellular virus particles. These clones lack detectable amounts of the mature gag proteins and accumulate large amounts of the Pr55 gag precursor; some also lack reverse transcriptase activity. Clones producing the non-infectious particles cannot be superinfected by infectious HIV. Purified and lysed whole virus preparations have been shown to lack an intact protease; the addition of protease isolated from a "wild-type" virus results in the degradation of Pr55 to intact mature gag proteins. These results suggest that the genetic defect may be in the protease gene itself. These HIV mutants might provide a useful model for the design of protease inhibitors.

MP.14 Helix Twist Angle Analysis of Retroviral LTR Sequences

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Degeneracy in the coding regions of genomic sequences can be analyzed in terms of "silent mutations" and conserved amino acid substitutions. In this study, we are exploring an analytical approach to degeneracy in non-coding DNA: the equivalent of a "silent mutation" is a base change that preserves the helix twist angle of the double-stranded DNA. A structural homology is a series of helix twist angles that are equivalent in two or more DNA sequences, irrespective of whether they happen to be sequence homologues.

Genomic LTRs (long terminal repeats) found at the 5' and 3' termini of retroviruses such as the HIV group, which utilize a trans-activating mode of control of viral replication in contrast to other LTR-directed mechanisms, offer an interesting class of sequences for this study. In particular, the TAR region (trans-activating receptor or target) found downstream from the mRNA start site has been the focus of our attention.

With a very stringent criterion of structural similarity, one helix twist pattern can be identified in all human and simian viral TAR sequences, represented by the consensus sequence "ctccga." The pattern is found at the same position for the most part; however, it occurs at a different position in HTLV-I and visna virus, in the former as "ggccgc" and in the latter as "ctccgg." With exception of visna virus, this pattern is found only in certain non-primate viral LTRs at yet a third position, which encourages us to pursue this mode of comparative analysis.

MP.15 In vivo Transmission Studies with MnlV, a Primate Lentivirus Partially Related to HTLV-III

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A retrovirus has been isolated after co-cultivation of a lymph node from a pig-tailed macaque (M. nemestrina) that died with lymphoma in 1982 at the University of Washington Primate Center. This isolate, designated MnlV (M. nemestrina immunodeficiency virus) is partially related to HTLV-III, based on amino acid sequence homology and immunological cross-reactivity of the major gag protein, p28. 10^3 infectious MnlV particles from an end-point diluted virus preparation grown on HuT 78 cells were inoculated i.v. into two species of macaques (rhesus - M. mulatta and pig-tailed). All macaques (six animals) became viremic and MnlV could be readily isolated from their peripheral blood lymphocytes. Two of the six macaques have died with opportunistic infections, anemia and depleted $T4^+$ cells at 4 and 15 months after inoculation. All macaques developed high titers of antibodies to MnlV, except for the animal that died at four months.

In a second experiment, eleven young cynomolgus macaques (M. fascicularis) have been inoculated i.v. with MnlV isolated directly on human lymphocytes. Six of these animals had previously received vaccinia virus containing the envelope protein of HTLV-III and had antibody titers to gp120 and gp41. These animals are being monitored to examine whether the presence of HTLV-III antibodies protects against a subsequent challenge by the related virus MnlV.

MP.16 HIV verification testing:A comparative study of the immunoreactivity of a cloned envelope protein (qp 160) and commercially available viral lysate

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In most HIV antibody detection protocols, ELISA reactivity must be verified by one of several methods including immunoblot, indirect-immunoflourescence or radio-immune precipitation. In LCDC the immunoblot has been the standard verification assay with more than 25,000 sera having been tested. Deficiencies in the immunoblot which will be described include: the presence of contaminating, co-migrating cellular products (e.g. a 24k polypeptide of cellular origin), batch to batch variation in antigen quality - including the proportion of individual viral components and unusual patterns of antibody reactivity against viral specific polypeptides.

The envelope gene of HIV (LAV) has been inserted into a Baculovirus and a polypeptide of about 160k expressed in insect cells. The efficacy of this bioengineered product as a diagnostic reagent has been evaluated using an immunoblot format and a spot-blot variation of it. More than 500 sera have been analyzed by both the standard immunohlot using a commercially prepared viral lysate and the alternative procedures employing the cloned gene product. Sera that react with only a p24 antigen in an immunohlot are considered HIV antibody equivocal. 12 of 30 equivocal sera reacted with the gp160 protein. All 12 were confirmed as antibody positive by RIPA and 18 were antibody negative. Similarly all of the 20 sera that reacted with only HIV gp41 also recognized the gp160 envelope protein. Our data indicate that both the sensitivity and specificity of procedures employing the cloned gp160 exceed those of protocols which rely upon a commercially prepared viral lysate.

MP.17 Neutralizing antibodies and cellular immune response in goats immunized with native envelope gp120 or with recombinant envelope proteins.

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Goats were immunized with native gp120, purified from HTLV-IIIB infected cells or with recombinant peptides representing various parts of the HIV ENV gene and produced in E. Coli or in an insect cells. Neutralizing antibodies were looked for by assessing the ability of the sera to prevent cytolytic action of HIV on a sensitive target cell, ATH-8. Cellular immune response to HIV was studied by assessing the proliferative responses of T cells stimulated with whole heat killed HIV, purified gp120 or with the recombinant peptides. Native gp120, two nonglycosylated recombinant peptides produced in E. Coli (PB1 and 5-90) and a glycosylated envelope protein produced in insect cells all elicited neutralizing antibodies. If the recombinant protein contained sequences from gp41, the neutralizing response was group specific, otherwise only type specific antibodies were seen. A group specific cellular immune response to three HIV isolates were seen in animals immunized with glycosylated native gp120 or with the recombinant glycoprotein from insect cells. The results suggest, that in spite of the great variability observed in the external envelope of HIV, vaccines representing one isolate may elicit a broad, group specific protective immune response.

MP.18 Preliminary Clinical Trial of Anti-Alpha IFN in Patients with AIDS: A Possible Approach for Immune Enhancement.

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Based upon the hypothesis that acid-labile alpha IFN may down-regulate the immune system (Skurkovich, S.V., Skurkovich, B. and Bellanti, J.A., Clin. Immunol. Immunopath., 1987, in press), a study was performed to evaluate the safety and clinical efficacy of anti-alpha IFN in patients with AIDS. Two patients with CDC-defined AIDS who had recovered from P. carinii pneumonia, received three daily intramuscular injections of sheep anti-alpha IFN immunoglobulin (1.5 to 9 x 10^6 I.U./day respectively) for a 6-day period during which time and subsequently thereafter (3 months and 3 weeks, respectively), clinical and laboratory parameters were evaluated. Although no serious adverse or toxic effects were observed following treatment, both experienced a mild maculopapular exanthem on the 9th to 10th day which disappeared within a week. In both patients on the 3rd day a mild transient lymphopenia was observed which disappeared by the 6th day. Following treatment both patients had a sense of well being; patient #1 experienced an 8 lb weight gain within 14 days of treatment. Before treatment both patients had detectable serum levels of acid labile alpha IFN (125 IU/ml). During the 6-day treatment period no IFN could be detected in the blood of either patient. However, 7 days after the cessation of treatment serum IFN levels in patient #1 increased to 630 IU/ml which was predominantly gamma IFN. Although the results thus far are promising and suggest the approach is feasible with negligible side effects, the long term efficicacy of anti-alpha IFN in AIDS will require further studies of dosage and frequency of administration.

MP.19 Herpesviral Transactivation of the Human Immunodeficiency Virus (HIV) Long Terminal Repeat Sequence.

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During the course of infection with HIV many individuals became coinfected with a variety of microorganisms. Since some of these pathogens may act as cofactors capable of stimulating HIV expression and thus accelerate disease, we examined one common coinfecting pathogen, herpesvirus type-I (HSV-1), for its ability to increase HIV gene expression. When an HIV LTR clone linked to the indicator gene chloramphenicol acetyl transferase (CAT) was transfected into Vero or SW480 cells, then infected with HSV-1, a 25-fold stimulation of CAT activity was observed. This effect was further increased by transfection of HIV tat DNA into cells subsequently infected with HSV-1. In cotransfection experiments of HIV LTR-CAT or an infectious molecular clone of HIV and recombinant plasmids containing three HSV-1 immediate early genes, segments encoding ICP0 and ICP4 stimulated CAT expression or reverse transcriptase activity while ICP27 had no effect. Analysis of HIV LTR deletion mutations revealed that the target of the HSV-1 encoded products was distinct from that responsive to the HIV tat gene. Primer extension experiments demonstrated a transcription component to the HSV-1 transactivation.

MP.20 Membrane Fusion Activity and Entry of HIV-1

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Internalisation of enveloped viruses into cells proceeds by one of two mechanisms. Some viruses (e.g. Sendai) fuse with target cell plasma membranes in a pH-independent manner. For others, however, (e.g. influenza, VSV), the fusion is pH-dependent. In these cases virions are internalised by receptor-mediated endocytosis and fuse with endocytic vesicles (endosomes) to release the nucleocapsid into the cytoplasm. The low pH triggers a conformational change in the viral spike glycoprotein which renders them fusogenic.

We have ascertained whether HIV-1 follows either of these mechanisms of entry. Weak bases (e.g. amantadine, NH_4Cl) and carboxylic ionophores (e.g. monensin), which have been shown to inhibit the entry of pH-dependent viruses do not inhibit HIV-1 entry into $CD4^+$ C8166 cells. Prolonged incubation in NH_4Cl does, however, reversibly inhibit the production of infected virus, both in C8166 cells and in chronically infected H9 cells. Furthermore, the entry of VSV (HIV-1) pseudotypes is not inhibited by NH_4Cl, even though non-pseudotype VSV is inhibited. These data suggest that HIV-1 induced membrane fusion is not dependent on low pH but that weak bases affect the maturation of virions. Immuno-electron microscopy for the CD4 antigen on C8166 cells indicates, however, that receptor-mediated endocytosis may be a method of internalisation of the virion-complex.

MP.21 A Simple Method for Detecting HIV-Antibodies Hidden in Circulating Immune Complexes

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In early and late (AIDS) stage of HIV infection ratio of HIV-antibodies to antigens may be near to equivalence with no free antibodies in blood. In these periods negative or doubtful reaction can be expected in anti-HIV assays.We have worked out a method for detecting HIV-antibodies hidden in immune complexes. Immune complex-enriched fractions were prepared from the sera tested by PEG precipitation.F(ab')2 fragments were released from complexed antibodies by low pH pepsin treatment.HIV antibody activity of the F(ab')2 fragments was compared to that of the original PEG precipitates using plates of Vironostika anti-HTLV-III kits as solid phase antigen. Antibodies fixed to the plates were detected either directly by a peroxidase-labelled anti-human κ-λ-antibody or by a competitive assay, measuring the fixation of HIV-antibodies to plates pretreated by F(ab')2 or PEG precipitate. Using both methods significantly higher antibody activity was found in F(ab')2 fragments than in the original PEG precipitates in 9/10 sera of confirmed anti-HIV positive patients.Therefore, our method seems to be suitable for detecting HIV-antibodies hidden in immune complexes.

MP.22 Regulation of HIV Long Terminal Repeat (LTR) Activity.

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The HIV LTR contains regulatory sequences that modulate viral gene expression. In order to delineate the sequences responsive to the viral tat protein, a series of mutations in the LTR tar region have been constructed employing deletion mutations and synthetic oligonucleotides. When tested for their ability to drive the expression of the chloramphenicol acetyl transferase (CAT) gene in the presence of tat, it was observed that LTR sequences lying between +37 and +62 were required for tat responsiveness. Additional mutations in the tar region are currently being studied both by CAT assays and in reconstructed viral genomes.

Expression of the HIV genome may also be regulated by cellular transcriptional factors. We have been studying the activation of HIV expression in U1 cells, a cloned macrophage cell line containing integrated proviral DNA and expressing low levels of viral RNA. When U1 cells are treated with the supernatant from lipopolysaccharide (LPS)- induced macrophages, viral RNA levels increase approximately 40-fold. Thus, stimulated macrophages may produce factors that transcriptionally activate quiescent HIV proviruses, presumably by altering the cellular transcriptional milieu of latently infected cells. The ability of purified monokines to augment HIV transcription in infected cells is being studied and the location of LTR sequences required for this activation is being analyzed employing HIV LTR segments mutated in the tar region and in upstream regulatory elements.

MP.23 Structure/Function Studies of Cloned HTLV-III/LAV from Zairian and French Individuals

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Different isolates of HTLV-III/HIV, the etiological agent of AIDS have extensive genomic diversity in nucleotide sequence with greatest divergence centered in the env regions and the most conserved regions in the gag and pol genes. Mechanisms which generate such diversity may allow the virus to survive host immune surveillance. Consistent with this, variants have been selected for when the virus is grown in vitro in the presence of neutralizing antibodies. To better understand the genetic divergence responsible for this phenomenon and to prepare additional reagents which may be useful for vaccine development it is necessary to study a large number of HTLV-III/HIV isolates. We have isolated and cloned viruses from two individuals with AIDS, one from Zaire (JY-1) and one from France (JY-2). The clones were obtained by isolating 9 Kb HTLV-III SstI fragments stretching from the 5' leader to the 3' LTR from phage lambda libraries. Comparison of the restriction enzyme maps of JY-1 and JY-2 and a prototype earlier American isolate, BH10, show that the 5' gag and pol regions share 10 of 12 sites while the 3' portion is less well conserved with 7 of 11 sites in JY-1 and 7 of 11 for JY-2. JY-1 appears to be more closely related to the American isolate than previously described Zairian isolates (Benn et al., Science 230, 949). Substitution of the protein coding regions of these viruses into the biologically active clone pHXB2-d yielded clones which produced virus after transfection into Cos-1 cells. Nucleotide sequencing is in progress.

MP.24 Suppression of AIDS Virus Replication in vivo by D-Penicillamine

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D-penicillamine (DPA) has been shown to inhibit HIV (HTLV-III/LAV) replication in-vitro (Chandra and Sarin, Drug Res. 36: 1, 184, 1986). It was therefore of interest to assess the in-vivo activity of DPA on virus replication in HTLV-III-infected patients with generalized lymphadenopathy (LAS) or ARC. Patients were treated on a high-dose regimen (0.5g escalating to 2g), or a low-dose schedule (0.5g daily) for 2 weeks to 4 months. A suppression of virus replication was observed in all cases, however the intensity of this inhibition was dependent on the dose schedule and the duration of treatment. In patients treated at low dose, the inhibitory response was in the range of 30-50%, which was reversed after two weeks of treatment termination. Three of five patients treated at high dose showed a complete inhibition of viral replication, and this suppression of HTLV-III replication persisted up to 24 weeks after the treatment was stopped.

MP.25 Nucleotide Sequence of an Active tat cDNA Clone of Simian T-Lymphotropic Virus Type III

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The human T-lymphotropic viruses shared, among other common properties, the ability to regulate their own expression mediated by transacting viral regulatory proteins. The prototype AIDS virus, HTLV-III/HIV, has at least three positive transactivating genes (tat-III, trs and sor) operating at various stages of virus expression. Recently, a second subgroup of primate retroviruses related to HTLV-III/HIV has been identified. The prototype of this subgroup is the simian T-lymphotropic virus type III (STLV-III$_{AGM}$) isolated by Kanki et al., from African green monkeys. In order to understand the transregulatory function of this new virus subgroup, we cloned and sequenced a functional transactivating cDNA from STLV-III. The complete cDNA clone is 2049 nucleotides in size. It comprises 4 exons and three open reading frames. These are analogous in position and size to the tat, trs and 3'-orf genes of HTLV-III. Alignment of the putative STLV-III tat gene with tat-3 revealed a highly conserved core sequence which likely represents the functional domain. We assayed the transactivating capacity of our cDNA clones by co-transfection with a plasmid pSV2CAT containing the putative transactivation target sequences (TAR) of the STLV-III LTR upstream of CAT. It showed marked transactivating function and this function is maintained when we substituted pSV2 CAT with the corresponding construct with HTLV-III LTR. We conclude that this new subgroup of primate retroviruses are similar to the HTLV-III/HIV viruses in their genomic organization and strategy for gene regulation.

MP.26 Transactivation of Human Immunodeficiency Virus by Herpesviruses

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We examined the interaction of human immunodeficiency virus (HIV) and herpes group viruses. For this purpose, a chimeric plasmid (pLTR-CAT) was constructed in which the long terminal repeat (LTR) sequences derived from a molecular clone of HIV were fused to a bacterial chloramphenicol acetyltransferase gene (CAT). Transient expression assays in transfected tissue culture cells were used to monitor the activity of the LTR. Basal levels of CAT activity were measured in HeLa and human lung fibroblast (HLF) cells transfected with pLTR-CAT. When HeLa or HLF cells transfected with pLTR CAT were infected with herpesviruses, HIV-LTR directed expression of the CAT gene was detected. Activation of HIV-LTR directed expression of CAT was observed for herpes simplex viruses (HSV-1 and HSV-2), cytomegalovirus and varicella zoster virus. Activation of CAT expression directed by the LTR was observed by cotransfection of subgenomic fragments derived from HSV-1, HSV-2, and CMV genomes. We have also constructed a series of recombinant plasmids containing deletions and multiple point mutations in the HIV-LTR sequences linked to the CAT gene. HeLa cells were transfected with such plasmids and followed by superinfection with herpesviruses to identify the sequences required for transactivation by herpesviruses. HIV-LTR directed expression may be a useful model for studying the effects on HIV of various infectious agents known to be present in individuals with AIDS or HIV infection.

MP.27 SIV/SMM: Prevalence and Association with Disease in a Breeding Colony of Mangabey Monkeys.

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A colony of mangabey monkeys at the Yerkes Center has a high incidence of infection with SIV/SMM, a T-lymphotropic retrovirus that is morphologically identical and serologically related to HIV. This colony, established in 1969 with wildborn mangabeys, currently consists primarily of lab-born animals. There has been no difference in the incidence of disease in the mangabeys as compared to other species at Yerkes. Twenty-six of 76 deaths (34%) were due to clinical diseases, including enterocolitis, pneumonia, amyloidosis, septicemia and meningitis. Candidiasis, lymphadenopathy and splenomegaly were rarely encountered. Two neonates were found to have a herpetic (CMV) glomerulitis. Two recently encountered diseases in mangabeys, amebiasis and necrotizing gingivitis (noma), suggest that the virus infection may be associated with clinical disease and death. Amebiasis occurred in an 11-year-old female; noma occurred in a 5-month-old infant. Both animals were seropositive for SIV/SMM and virus was isolated from blood and multiple tissues from both cases, including the brain from the noma case. Although 88% of the adult mangabeys checked have been virus positive, this is the first virus isolation from an infant. The high infection rate in mature animals and occurrence of infection in an infant suggests that transmission of SIV/SMM may be comparable to the transmission of HIV (sexually or perinatally). This colony of naturally infected mangabeys may, therefore, serve as a model system for study of the epidemiology and pathogenesis of an HIV-like retrovirus, and for identification of cofactors that may be associated with the occurrence of AIDS (supported by NIH grant no. RR-00165).

MP.28 Structural Relationship between Core Polypeptides of Human and Simian Immunodeficiency Viruses as determined by Peptide Mapping

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Simian immunodeficiency viruses (SIVs) are serologically and biochemically related to the human immunodeficiency virus type 1 (HIV-1) the cause of AIDS. The SIVs isolated from macaques (SIVmac) and sooty mangabey (SIVsm) induce an AIDS-like disease in rhesus monkeys. Recently, two novel human retroviruses, HIV-2 and HTLV-IV, were found in West Africa. They are antigenically more related to SIV than to HIV-1. In order to classify HIV and SIV isolates, we have compared tryptic peptide maps of the core polypeptides p18 and p24 of HIV-2, three HIV-1 and five SIV isolates. Peptide maps of all isolates are distinguishable. Differences appear to be most prominent between the two groups of HIV-1 isolates and SIVmac/SIVsm. HIV-2 is very similar to SIVmac and SIVsm. SIVs of African green monkeys (SIVagms) are the most heterogeneous group. The core polypeptides of one SIVagm isolate is more related to HIV-1. The two other SIVagms also resemble more to HIV-1 with respect to their p24s, but their p18s are more similar to those of SIVmac /SIVsm/HIV-2 than to those of HIV-1. Therefore, two SIVagm isolates could be gag gene recombinants between human and simian viruses or their ancestors.

MP.29 Biochemical Features of the 3'orf Gene Product of HTLV-III/HIV
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We previously identified a 27kd protein (p27) from an HTLV-lIIb infected cell line which was immunoreactive with antibodies from infected people and encoded by the 3'orf gene by amino acid sequence analysis. We have extended our studies to learn more of the biochemical characteristics of p27 in the hope of gaining some insights into the functional aspects of the 3'orf gene. Initially, levels of expression of p27 were evaluated among different HTLV-III/HIV isolates and those of STLV-III and HTLV-IV using radioimmunoprecipitation (RIP) techniques. It was found that multiple species of p27 exist in some cell lines which range in molecular weight from 26kd to 30kd. Additionally, p27 is modified by fatty acid myristylation as detected by 3[H]myristate incorporation and a similar species (p33) was found to exist in STLV-III and HTLV-IV infected cells indicative of a conserved 3'orf gene product. P27 was shown to be cell-associated and cerulenin, an inhibitor of lipid metabolism, was found to alter the migration of p27 by SDS-PAGE suggesting that this species represents the nascent polypeptide.

Although greater than 20% amino acid variability in the 3'orf gene is seen between some isolates, highly conserved regions exist and from a search of gene bank sequences we observed limited amino acid homology with E1B, an early adenovirus gene involved in tumorigenesis. These homologous sequences were confined to the conserved regions between HTLV-III/HIV isolates suggesting either structural or functional constraints in the evolution of the 3'orf gene.

MP.30 Expression of Large Amounts of Native and Mutated Forms of the HIV Envelope Proteins Using a SV40 Late Replacement Vector
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An eukaryotic expression vector producing large amounts of the HIV envelope proteins (gp 160/120) has been constructed by introducing the Sal I/Xho I fragment from the BH10 isolate into a SV40 late replacement vector. The vector is a shuttle vector that replicates to high copy numbers in both E. coli and eukaryotic cells permissive for SV40 replication.

Transfection of the HIV recombinant into CV1 monkey cells gave high levels of expression of gp 160 and gp 120 in approximately 30% of the transfected cells. By several criteria the proteins were indistinguishable from those produced during infection. The proteins were localized to both the cytoplasm and the plasma membrane and some of the gp 120 was shed into the culture medium. Approximately 0.5 ug of envelope protein could be extracted from 10^6 cells. Thus this transient vector system provides an abundant source of native envelope protein for purification and characterization.

In addition several recombinants designed to express mutated forms of the envelope proteins have been created.

MP.31 Simple, Rapid, Quantal, Syncytium-Forming Micro-Assay for the Detection of Neutralizing Antibody Against Infectious HTLV-III/LAV.
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A need for a simple, rapid, quantal cell system for the sensitive detection of neutralizing antibodies and evaluation of various antiviral agents against HTLV-III/LAV is well recognized. Herein is described a syncytial -forming assay that directly correlates with more complicated and cumbersome infectious virus assays. A syncytial sensitive clone of CEM cells was identified and made adherent to flat bottom 96-well microtiter plates. These cells exhibit one-hit kinetic syncytium formation at a multiplicity of infection of 0.005. These syncytium develop by 5 days on a confluent cell monolayer background and remain attached for easy quantitation. These syncytial foci are associated with complete virion production and focally positive p24 immunofluorescence. Five different HTLV-III/LAV isolates (IIIb, LAV, MN, RF11, and Rut-Z, including IIIb reisolated from persistently infected chimpanzees, produce quantifiable syncytium, which varied slightly in their morphology of formation. Various anti-HTLV-III/LAV sera from various species (man, chimpanzee, goat, equine, and rhesus) have been tested and found to contain titers comparable to immunofluorescent methods. Infectious virus can be accurately and rapidly titered in this assay and correlated to p24 and gp120 when microtiter well supernates are evaluated by competitive radioimmunoassay methods. This assay has the advantage of allowing numerous, small volume samples of either antiviral or suspect antisera to be tested in a rapid and sensitive fashion. Inherent with this system is a flexible method for studying various kinetics of antibody/viral interactions, blocking, and various interference studies.
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MP.32 In vitro produced factors promote the growth of Kaposi's sarcoma (KS) cells
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Epidemic HTLV-III related KS is an aggressive disease of young people and is a multifocal and histologically complex lesion consisting of spindle cells, endothelial cells and fibroblasts. So far, its origin and pathogenesis remain unknown. Here, growth of KS cells were compared to normal endothelial (NE) and fibroblast like (NF) cells. Cell growth was assessed by cell number, ^3H thymidine uptake and mitotic index. Conditioned medium from HTLV-II-transformed human T_4^+ cell lines (HTLV-II-CM) stimulated the growth of 6 of 6 KS cells as well as NE cells, but was much more potent for the growth of the KS cells. These KS cells, although slow growing, have been cultured with the help of this factor(s) for over 9 months, and large quantities of cells have been harvested for study.

Nine well known growth factors, including endothelial cell growth supplement (ECGS), basic fibroblast growth factor (FGF) and IL-1, were also tested for their growth promoting effects. ECGS and FGF induced the growth of NE and NF cells, but, they had little or no effect on the growth of KS cells. Conversely, IL-1 stimulated the growth of KS cells, although it plateaued early as compared to HTLV-II-CM and had little or no effect on NE and NF cells.In addition, molecular analysis revealed that the factor in HTLV-II-CM differed from ECGS and FGF, but whether it differes from other known lymphokines, including IL-I, is under investigation. In summary, we have developed an in vitro system for the study of KS. Our results show that KS cells have a different growth factor dependency than NE and NF cells. This system should provide further clues to our understanding of pathogenesis of KS.

MP.33 Comparative Structural Analysis of the Env Genes of Group B T-lymphotropic Retroviruses (STLV-III and HTLV-III)
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Recently viruses have been identified in monkeys in Africa which by serology are related to HTLV-III. They have been designated simian T-lymphotropic viruses, type III (STLV-III), and appear to cause an AIDS-like disease in macaques. Viruses related to STLV-III have been identified in healthy and apparently immunocompromised humans from West Africa. In order to compare STLV-III and HTLV-III and to try to identify common structural features which might explain their similar pathobiology, we determined the complete nucleotide sequence of the env gene of STLV-III. The overall nucleotide sequence homology to HTLV-III is 52%. The homology of the inferred amino acid sequence of the env protein to that of HTLV-III was 34%, substantially greater than to those of the lentiviruses visna (15%) and equine infectious anemia virus (14%). The small transmembrane env proteins were more closely related (40%) than were the external large envelope proteins (30%). Regions of homology between these env gene products tended to cluster within regions which are relatively strongly conserved among different HTLV-III isolates. This suggests that these code for genetic determinants which are of functional importance to parts of the viral life cycle, such as binding to the T4 receptor protein. In addition, there is a remarkable conservation of cysteine residues (2 out of 23 cysteine residues in the HTLV-III env proteins are also present in that of STLV-III). This strongly suggests that they play a critical role in establishing or maintaining the proper conformation of the viral envelope. Other aspects of this work will be discussed.

MP.34 HTLV-II in Patients with AIDS and Lymphoproliferative Diseases: Isolation and Characterization.
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HTLV-II was previously isolated from two patients with variants of hairy-cell leukemia (1,2) and one hemophilic patient with AIDS (3). However, recently serological (4) studies indicated that HTLV-II might be more widely disseminated. During the process of screening patients for antibody to HTLV-I/II and HTLV-III, several with diseases not previously associated with HTLV-I infection were found seropositive for HTLV-I/II. A retrovirus was isolated from peripheral blood or lymph node leukocytes of six of these selected patients which, upon further characterization, proved to be HTLV-II. Two patients with a history of intravenous drug abuse, diagnosed with dermatopathic lymphadenopathy, had concomitant infection by HTLV-II and HTLV-III. HTLV-II was also isolated from one patient with prolymphocytic leukemia and from three patients with hairy-cell leukemia. These and previous observations demonstrate that in addition to its' association with, at least, some variants of hairy-cell leukemia, HTLV-II is more widely disseminated and possibly associated with other malignancies.

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MP.35 Analysis of Sera Exhibiting Atypical Reactions With HIV

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During clinical trials of a screening assay for antibody to HIV (Genetic Systems LAV EIA), a small number of atypical sera (n=6) were identified which were positive by EIA, negative by radioimmunoprecipitation (RIP), and positive only with single core antigens p25 or p18 (with or without precursors p55 and p40) by Western blot. A study was initiated to collect and characterize a larger sample group in order to assess the significance of this reactivity. In total, 91 atypical samples were analyzed. Twenty-five samples reacted with p25, 42 with p18, 19 with p18 and p24, 4 with p25 and p34 and one with p18 and p34. In nine individuals where sequential samples were available, no significant changes in serum reactivity were observed over 6 mos. to 2 yrs., arguing that these samples do not represent seroconversions. Viral cultures attempted from cells of nine individuals were negative when analyzed by fluorescence, RT assays and antigen capture. Futhermore, no reactivity to STLV-III, HTLV-I, or LAV-II viral antigens was found in 26 samples tested. These results suggest that Western blot reactivity with core antigens alone, in the absence of RIP reactivity, does not indicate prior exposure to HIV. Atypical sera were further analyzed using a prototype second generation ELISA which incorporated synthetic peptide antigens containing sequences from ENV, (gp41), GAG (p25) and POL (p34). Only 5.5% (5/91) of atypical sera reacted in this assay, whereas a similar assay using E. coli recombinant p25 and p18 antigens detected 61% (16/26) of atypical sera. Immunoassays based on peptides may therefore offer the opportunity to significantly reduce false positives attributable to the reactivity of atypical sera.

MP.36 Analysis of the Reactivity of Human Sera to a HIV env Region Capable of Eliciting Neutralizing Antibodies in Animals Using Synthetic Peptides

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Recent studies indicate that portions of the HIV env open reading frame encode protein sequences which can elicit neutralizing antibodies in goats. We have analyzed the reactivity of HIV positive human sera to these regions using overlapping synthetic peptides. A rapid peptide synthesis method was used to make overlapping peptides covering the entire gp120 region. Peptides of 15 to 16 amino acids with 5 overlapping amino acids on each end were made. Seventeen peptides, covering a region of IIIB previously shown to elicit neutralizing antibodies in animals (PvuII-BglII), and thirteen peptides covering the same region of an envelope variant strain RF, which had sequences different than IIIB, were tested. Peptides were immobilized on ELISA plates directly by glutaradehyde and analyzed using normal and HIV ELISA positive sera. Three peptides from IIIB reacted strongly with 30-40% of the HIV ELISA positives. Selected sera were fractionated on affinity columns made of reactive peptides and the activity of eluted antibodies was assessed. In addition peptide conjugates were injected into guinea pigs; and the ability of anti-peptide antibodies to react with viral proteins and/or inhibit infectivity was tested. The results of these experiments will be discussed.

MP.37 HIV Related Sequences in Insects from Central Africa

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We have studied the presence of HIV related sequences in more than 200 insects from endemic area for AIDS in Central Africa. This analysis has been performed using squash blot, dot blot and southern blot techniques. Viral sequences have been found among insects from urban or suburban area, directly or indirectly in contact with humans. Positive insects included mosquitoes, antlions tsé-tsé flies, cockroaches, ticks and bed-bugs. Squash blot analysis indicated that up to 30 % of mosquitoes from endemic area contained such viral sequences. Studies on mosquitoes also suggested a transovarian transmission of the viral genes since positive results were observed both with males and females. Insects with specialized feeding such as termites or crickets were constantly found negative. Flies, bees, day-flies from Paris area were also negative. The specificity of the hybridization signals has been confirmed using several probes as negative controls. Such controls included hybridization with pUC18, Kappa globulin, HTLV1, type D SRV and M-MuLV probes. Hybridization with subgenomic HIV1 probes also indicated that most of the viral genes are present in positive insects. However the restriction patterns observed by southern blot analysis is not similar to the one obtained with the prototype HIV1 strain. These results suggest that insects might be contaminated by infected human material and thus could be carriers of HIV genes but not vectors as clearly evidenced by previous epidemiological studies.

MP.38 Cerebrospinal Fluid (CSF) Studies in Adult and Pediatric HIV Infections

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Studies of cerebrospinal fluid (CSF) in virus-positive adult and pediatric patients were compared. The groups included 11 adults (20 specimens) enrolled in a trial evaluating 3'-Azido-3'-deoxythymidine (AZT) and placebo and 14 children (19 specimens) with HIV infections in whom lumbar punctures were done because of fever and possible sepsis. Sequential isolation attempts from CSF were made from 2 children and 7 adults. All patients were repeatedly virus-positive from peripheral blood leukocytes and all had HIV-associated clinical disease. All children had delay in growth and/or developmental milestones and 2 had progressive neurological disease. HIV was recovered from the CSF of only 4/14 (29%) children. Neither of the children with progressive neurological disease was CSF virus-positive. CSF cell count and protein were normal in 3/4 children with positive and 7/10 children with negative cultures. CSF cultures for HIV were positive in 8/11 (73%) adults including 3 patients on multiple occasions. Although the CSF cell count was abnormal more often in virus-positive (100%) than virus-negative CSF (46%), cell counts even in virus positive CSF were only slightly elevated (mean - 9 lymphocytes/ mm^3). There was no significant difference in the proportion of virus-positive and virus-negative CSF with elevated protein, 62% (mean 57 mg/dl) and 50% (mean 52 mg/dl), respectively. Patients with virus-positive CSF culture only became negative in patients receiving AZT (2/4). HIV is more readily recovered from the CSF of HIV-infected adults than children even if neurological abnormalities are present in the pediatric patients. The usual parameters of inflammation, elevated cell counts and protein, apparently are not predictive of the presence of virus.

MP.39 Interaction between GP 120, the Major Env Protein of HIV, and CD4: Binding Region in GP 120 and Role of Carbohydrates.

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The interisolate variation of the env region of HIV is one of the major problems for the production of an AIDS vaccine. In order to find a conserved CD4-binding region in GP 120 we have performed enzymatic digestion of this protein for subsequent testing in a simple binding assay developed in our laboratory. Two fragments were found to bind to the CD4 receptor. Preliminary analysis of these fragments indicates that the bindingsite in GP 120 is located in the carboxyterminal region. Deglycosylated GP 120 (DG 120,MW 58-60) has been shown to bind to the CD 4 receptor with much less avidity than GP 120 in its native form. Further studies including kinetics of the deglycosylation of GP 120 were carried out and revealed a significantly different efficacy depending on the enzyme used. DG 120 was tested in our binding assay. Our conclusion is that carbohydrates stabilize the peptide configuration necessary for CD 4 binding to occur.

MP.40 Experimental assessment of bedbugs and mosquitoes as vectors of Human Immunodeficiency Virus (HIV)

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In vitro experiments were conducted to assess whether the common bedbug (Cimex lectularius), the tropical bedbug (Cimex hemipterus) and the mosquito (Aedes aegypti) could act as vectors of HIV. The insects engorged through a membrane on a blood-virus mixture. At various intervals after feeding insects were killed, stored at -70°C and subsequently tested in pools of 5 for reverse transcriptase activity. This was done by inoculating each insect extract into H9 lymphocyte cultures, passaging the cells for 3-6 weeks and then testing culture supernatants for reverse transcriptase activity. HIV was thus shown to survive in C. lectularius for up to 4 hours, in C. hemipterus up to 1 hour but to remain undetectable in Ae. aegypti. Four attempts to transmit HIV by interrupted feeding, using groups of 100 C. lectularius, from a blood-virus mixture to uninfected blood failed. It is concluded that Ae. aegypti and probably other mosquitoes are not vectors of HIV. The results also tend to discount transmission by bedbugs. However, the survival of virus in bedbugs, especially in C. lectularius, would permit the bugs to transmit HIV mechanically between humans under natural conditions provided interrupted feeding were to occur and the virus was sufficiently infectious. Whether the former occurs is unknown but HIV is known to have a low infectivity.

MP.41 HIV Infection in Drug Addicts : an Epidemiological Study in Turin, North Italy.

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In 1985 we undertook a survey to estimate the prevalence of HIV infection and the risk factors associated with seropositivity in drug addicts (DA) attending the N.H.S. Centers, Turin.

All 320 subjects enrolled were IV heroin abusers on different treatments. Mean age was 26.4 (S.D. 4.56), 78% males and 22% females. The prevalence of HIV antibody was 28%, slightly higher in females. The highest seroprevalence was in the 20-24 age group with a trend to decrease in older ages. Seroprevalence increases with duration of addiction up to 9 years, beyond which it decreases.

In spite of free sale and large availability of syringes in Italy, needle sharing was referred by 81% of interviewed DA. The relative risk (RR) of this practice was 4.07 (C.L.95%: 1.46-12.25); 3.63 for occasional sharing (1.28- 11.08) and 6.10 for frequent sharing (1.82-20.81). Needle sharing in prison was reported by more than 30% of DA with history of imprisonments.

Detailed sexual history demonstrated a correlation between number of partners/year (P/Y) and seropositivity (RR 1.83 for 3-10 P/Y; RR 1.90 for 11-50 P/Y; RR 4.65 for 51 P/Y). Standardization for sex and/or needle sharing confirmed this association. Having a steady partner, even if DA, appeared to be protective. Homosexuality was infrequently reported and not associated with seropositivity.

At clinical examination, 3 or more enlarged lymphatic sites were found in 20.4% of DA (64.8% of these were positive). RR of being positive in presence of lymphadenophathy was 10.34 (4.73-24.37).

Since needle sharing and number of sex partners seem to be the most important risk factors in DA and seroprevalence in Turin is still low compared to other italian cities, a timely and well planned control program could limit the spread of HIV infection. A follow up, now in course, will determine the impact of this policy."Free needles" cannot be the mainstay in preventing HIV spread among DA.

MP.42 HIV ANTIBODY PREVALENCE IN BLACK MINERS BETWEEN 1970 - 1974

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Between 1970 - 1974 a pneumococcol vaccine trial was conducted in black mine workers in South Africa. Aliquots of serum collected during this trial were stored at -20°C. In November 1986 these sera were tested for antibodies to HIV. Participants in the trial came from Mocambique (1191), Malawi (1080), South Africa (171), Lesotho (55), Botswana (32), Angola (29) and Swaziland (16). As initial screening with the Abbott HTLV-111 EIA gave many false positives, all sera were tested with the Wellcozyme anti-HTLV-111 and positives were confirmed with indirect fluorescence, Elavia-EIA and Western Blotting. Eleven sera were found to be positive with the Wellcozyme test, six of which were positive with indirect fluorescence. These sera were negative with Elavia and Western Blotting Two sera, positive with Abbott EIA and indirect fluorescence but negative with Wellcozyme and Elavia, gave moderate staining with Western Blotting to P17, 24, 35, 55, 56 and GP41 and 120. One was from Malawi and the other Lesotho. This study fails to provide convincing evidence of HIV infection in Malawi, Mocambique and other Southern African countries between 1970 - 74. In a comparable group of mine workers surveyed in 1986 the prevalence of HIV infection was found to be 3.71% in Malawians and 0.07% in Mocambicans.

MP.43 TRANSFUSION-ACQUIRED HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION in NEONATES.

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Eleven neonates received blood from two HIV infected donors. All developed laboratory and/or clinical evidence of HIV infection, usually in the first year of life. Nine of 11 had serum antibody to HIV when tested between 9 and 16 months of age; two seronegative infants were severely hypogammaglobulinemic when tested. Nine patients developed a variety of illnesses characterized by hepatosplenomegaly, lymphadenopathy, chronic diarrhea, failure to thrive, and thrombocytopenia. Infections, including pneumonia, mucocutaneous candidiasis, and sepsis were a major source of morbidity and mortality. Two children have remained continuously asymptomatic. In follow-up ranging from two to four years, five patients have died, four others had HIV associated illnesses, but recovered and are now healthy. All patients had immunologic abnormalities; the most consistent finding was a decreased proportion of T-helper cells. Three patients had panhypogammaglobulinemia. These infants had significantly lower numbers of T-helper cells compared to patients with normal or increased serum immunoglobulin concentrations (P=0.012). We conclude that exposure to HIV via transfusion in the neonatal period results in an extremely high rate of infection with substantial mortality and morbidity, but clinical recovery occurs in some patients. Second, hypogammaglobulinemia may be more common in infants with HIV infection than previously appreciated.

MP.44 Status of AIDS in the Americas

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In 1983, the Pan American Health Organization initiated regionwide surveillance for AIDS. Because AIDS was confined almost exclusively to the United States, a very simple reporting system was installed based on the Centers for Disease Control's case definition. Member Countries were requested to report the total number of cases of AIDS and deaths due to AIDS every six months. The objective was to follow the spread of AIDS within the Region.

This report summarizes the available data based on the PAHO surveillance system, as well as data from several special studies carried out in some of the countries. The data are sufficient to define the overall picture of AIDS in the Americas, although the exact magnitude of the AIDS problem is not known precisely in each country.

The occurrence of opportunistic infections as markers for AIDS is variable throughout the Region. With some exceptions, the specific frequencies of certain infections are essentially the same as in the United States. Diarrhoeal illness is more common in Haiti and generalized Mycobacterium tuberculosis infection is more common in Brazil and the Dominican Republic.

The homosexual/IV drug user patient profile common in the United States (Western AIDS) prevails in Latin America and the Caribbean, with a greater proportion of homosexual and bisexual men and a much smaller proportion of intravenous drug abusers. In the Americas, AIDS is predominantly a sexually transmitted disease.

AIDS is a growing problem in the Americas, whose overall pattern, with the exception of Haiti, appears to be following the pattern established in the United States.

(Source: Health Situation and Trend Assessment Program (PAHD).

MP.45 Prognostic value of HIV antigen capture assay in a long-term prospective study of seropositive hemophiliacs.

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Ninety-six hemophiliacs positive for HIV antibody entered a 28+6 month prospective study. Every 4-6 months they were monitored for clinical and biological parameters including 3 HIV markers: HIV antigen (HIV Ag), p24 and gp41 antibodies (Ab). Eight subjects were HIV Ag positive at entry and 14 became positive during the study 7-47 months after seroconversion. HIV Ag containing samples had low titer or undetectable p24 Ab but high titer gp41 Ab. In the HIV Ag negative group, 66 subjects had high titer of both p24 and gp41 Ab and 8 had low p24 Ab titer and high gp41 Ab titer over a 2-3 year period. Clinical comparison between the 22 HIV Ag positive and 56 HIV Ag negative subjects showed a significant increase in AIDS cases (2/0 $p<0.05$), immunodeficiency related infections (7/1 $p<0.001$), immune thrombocytopenia (8/6 $p<0.001$) and severity of condition according to the Walter Reed staging system ($p<0.001$). In this group of mostly asymptomatic subjects at entry, neither T4+ lymphocytes nor T4/T8 ratio appear predictive of clinical severity.

These results strongly suggest that the detection of HIV Ag associated with low titer or undetectable p24 Ab is an indicator of HIV related clinical complications and could be used to select patients for entry in drug trials prior to the development of ARC or AIDS.

MP.46 Antibodies to Human Immunodeficiency Virus in Clinical Patients Presenting Mononucleosis-Like Syndrome.

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Serological tests were performed with sera of 434 patients clinically presenting a mononucleosis-like syndrome. Antibodies to Human Immunodeficiency Virus (HIV) were detected in 15 cases (3.5 percent). A close correlation of positive results was obtained among enzyme immunoassay, Western blot (performed in two different laboratories), immunobinding assay, complement-fixation and indirect immunofluorescence. The high degree of agreement among the results of tests using different methodologies contributes to the significance of these (unexpected) positive results.

HIV positive sera were also tested for other agents known to cause infections or be reactivated in immunocompromized hosts. Thirteen out of 15 were seropositive for Cytomegalovirus, 7/15 for Toxoplasma gondii, 15/15 for Herpes simplex virus, 15/15 for Epstein-Barr virus and 0/15 for human Polyoma virus. No IgM antibodies were found to the above agents, except for one with Epstein-Barr IgM, and one with border-line IgM to this virus. Syphilis serology was uniformly negative.

These results should encourage the testing of sera for HIV antibody in patients outside the so-called "risk groups". This is justified, even if the test is not requested, since it is the only way to accumulate more epidemiological data on the spread of this infection. Historically similar studies have been performed on many other infectious diseases with excellent results. HIV should be no exception.

MP.47 Perinatal HIV infection: preliminary report of prospective study on 71 infants.

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To define the natural history of perinatal HIV infection, three European Centres collaborated in a prospective study to determine the prevalence of infection in infants born to seropositive mother, and to document the clinical and immunologic outcome.

Seventy-one children were identified at birth, and seen 3 monthly. Twenty-seven (38%) have been followed up for longer than 8 months. Forty-eight infants were delivered vaginally, 21 by caesarean section. Breast feeding took place in 7 infants.

The clinical outcome in the infants could be grouped into the following: I - Asymptomatic (n = 60)

II - Non specific signs (n = 4) which included unexplained lymphadenopathy, hepatosplenomegaly, neurodevelopmental abnormalities.

III - HIV syndrome (n = 7). These infants presented with signs in II as well as recurrent/unusual infections, opportunistic infections, recurrent/protracted diarrhoea.

No correlation was seen between outcome and mode of delivery, or breastfeeding. We propose a uniform classification for HIV disease in infants and children, separate from the one currently used for adult disease.

MP.48 AIDS in developing countries

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Brazil, with a population of 136 millions inhabitants has, in 1986,the second largest number of AIDS patients in the world. Around one thousand cases were notified up to December 31,1986, sixty percent of such figures been notified in São Paulo. Considering the evident underreporting of infectious diseases and the fact that AIDS was not yet made compulsory for notification in this country, very probably such numbers should be raised 50-100%.

The perspectives for AIDS in Brazil, and as an extension in the 3rd World, are very peasimistic. Poor socioeconomic and cultural patterns of most of the population, added to poor housing, promiscuity and high prevalence of malnourished people allow us to raise such dark predictions. Preliminary serological H.I.V. antibodies surveys have shown 53% of homosexuals, 39% of tranevetites , 43% of haemophiliacs, 8% of renal haemodyalieis patients, 0.2-10% of blood donors, 2% of prostitutes and 100% of full-blown AIDS patients, to be positive .

Brazilian indians living in the border to Venezuela did not show any evidence of past infection with the H.I.V. Also, blood drawn from Brazilian Navy sailors in 1974, resulted negative for H.I.V. antibodies. Around 200.000 serological tests carried out in private blood banks in São Paulo city showed a 0.25% positivity. In Rio 0.36% tests among 14.756 blood donors resulted positive for H.I.V. antibodies. It was estimated that, in 1987, between 500.000 and one million Brazilians will be infected by the H.I.V. Based on an observation of one case of hepatic-splenic Schistosomiasis with AIDS we can speculate on the changing patterns of the histopathological pictures of a few endemic diseases such as Leishmaniasis, Chagas' disease, Malaria, Tuberculosis, Leprosy, Dengue, Yellow fever and Paracoccidioidomycosis.

MP.49 Risk of HIV Seropositivity in Relation to Specific Sexual Activities of Sexual Contacts of Men with AIDS or ARC.

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244 male sexual contacts of men with either AIDS or ARC were recruited into a prospective study between July, 1984 and July 1985. At induction, data were collected on the sexual relationship between the sexual contact and his primary case, as well as data relating to sexual activity with other men. At recruitment , 141 sexual contacts had antibodies to HIV while 103 were seronegative. All seronegatives had last had sexual exposure to their primary cases at least three months prior to antibody testing. After adjusting for the number of sexual encounters with primary cases and the number of other male partners, the following sexual activities with the primary case were significantly associated with seropositivity in sexual contacts: receptive anal intercourse (O.R. (odds ratio)=3.4 , p<0.0001); insertive anal intercourse (O.R.=2.3, p<0.01); receptive fisting (O.R.=4.3, p<0.01); receive a dildo in anus (O.R.=3.9, p=0.002); mutual masturbation solely (O.R.=0.45, p<0.05). Similar results arose when analysing data on sexual activities with men other than the primary case. Also, seropositivity was associated with sexual contact with men from U.S. centres (New York City O.R.= 2.4, p=0.003; Houston/Dallas O.R.=3.7, p=0.002). Further, logistic regression models which simultaneously adjusted for sexual activities with primaries and other men, revealed that seropositivity was significantly associated with only receptive and insertive anal intercourse with the primary cases and sexual contact with men from Houston or Dallas. All seropositive contacts had either receptive or insertive anal intercourse with primaries or other men. Oral sexual contact was never associated, significantly, with HIV seropositivity.

MP.50 Risk of HIV Seropositivity in Relation to History of STD's and Recreational Drug Use in Sexual Contacts of Men with AIDS or ARC.

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244 men who had had sexual contact with men with either AIDS or AIDS-related complex (ARC) were recruited into a prospective study between July, 1984 and July, 1985. At induction, data were collected on the sexual relationship between the sexual contact and his primary case, as well as data relating to sexual activity with other men, history of sexually transmitted diseases (STD's), and use of a variety of recreational drugs. At recruitment, 141 of the sexual contacts had antibodies to HIV while 103 were seronegative. All seronegatives had last had sexual exposure to their primary cases at least three months prior to antibody testing. After adjusting for number of sexual encounters with the primary case and other men, the following variables were associated significantly with HIV seropositivity in contacts: history of rectal gonorrhea (O.R. (odds ratio)=2.8, p 0.001); history of syphilis (O.R.=2.3, p=0.006); history of hepatitis (O.R.=2.9, p<0.0001); use of ethyl chloride (O.R.=2.8, p=0.007); use of 'uppers' (O.R.=2.3, p=0.006); and use of MDA (O.R.=2.4, p=0.004). Logistic regression models which controlled for confounding by specific sexual activities with the primary case and other men revealed that history of hepatitis, history of syphilis, and use of MDA remained significantly and independently associated with HIV seropositivity.

MP.51 The Epidemiology and Clinical Manifestations of AIDS in Israel.

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As of Dec 1,1986, 23 cases of AIDS have been reported to the Israeli Ministry of Health among persons residing in Israel. In contrast to the experience in the United States and Europe, rates of AIDS were low and have progressed slowly during the last four years (0.5 - 0.75 cases per million).

Risk factors for AIDS were identified in 22 patients: homosexuality in 12 , hemophilia in 8 and receipt of blood transfusions in 2. Eleven of the 12 homosexuals have, most likely, been infected abroad, and all hemophilia patients had received imported commercial clotting factors. The two cases associated with blood transfusions received blood donated in Israel.

The spectrum of clinical presentations and opportunistic pathogens was similar to that reported in the Western World, except for one case of Mycobacterium Simiae systemic infection. Seroepidemiologic studies in 1984-86 suggest a low prevalence (<10%) of HIV antibody among homosexuals and IV drug abusers.

Sexual relations abroad of persons at risk for AIDS and receipt of imported clotting factors are the most important risk factors for AIDS in Israel. Transmission of the virus among Israeli homosexuals seems to be infrequent at the current level of exposure to the virus. The low prevalence of HIV antibody in homosexuals and IVDA's suggest that Israel is a pre-epidemic area for AIDS.

MP.52 Assessing and Modelling Heterosexual Spread of the Human Immunodeficiency Virus in the United States

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Epidemiological investigation of the AIDS epidemic among heterosexuals has been chiefly of two types: 1) studies of partners of individuals infected with the Human Immunodeficiency Virus (HIV) and 2) population surveillance. Although heterosexual partners of infected individuals (including those without other risk factors) appear to be at high risk of infection, only a small proportion of total number of cases of AIDS have been attributed to heterosexual contact in the United States and Europe. To reconcile these findings, we develop an epidemic model for heterosexual spread of HIV infection and fit to surveillance data. Fitter parameter values are restricted to a range that is consistent with findings from partner studies. Because, at present, most HIV-infected heterosexuals and bisexuals have been infected through other means (IV drug use or homosexual contact), the model considers two interacting populations: a small population of individuals rapidly infected by high risk activity and a large population of individuals at risk only from heterosexual contact. No precise predictions concerning the future of the AIDS epidemic among heterosexuals is possible at this time, but current epidemiological findings do not appear to preclude a major heterosexual epidemic. Projections depend strongly on the delay between infection and infectivity. In addition to using the model for projection, it can also be used to examine the assumptions required for interpretation of results of case-control studies of HIV infection.

MP.53 HIV Antigenemia: Association with Decreased Numbers of T4-cells and Increased Risk for AIDS

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Sequential serum samples of 256 HIV antibody (HIV-Ab) seropositive and seroconverted homosexual men, participating in a prospective study on the prevalence and incidence of HIV infection and risk factors for AIDS, were tested for HIV antigen (HIV-Ag). Forty (20.2%) of 198 HIV-Ab seropositives were HIV antigenemic throughout the study period of an average of 19.3 (± 0.5) months. Among the remaining 158 HIV-Ab seropositive individuals and 58 HIV-Ab seroconverters 28 became HIV-Ag seropositive (attack-rate 14.3%). 114 (44.5%) of the 256 remained asymptomatic during the study period. Constitutional disease developed in 39 (15.2%) and was seen more frequently among HIV-Ag seropositive than among HIV-Ag seronegative individuals ($p < 0.00001$).

AIDS developed in 15 men; the AIDS attack-rate was 23.9% in the HIV-Ag seropositive and 1.3% in the HIV-Ag seronegative group ($p < 0.00001$; $O = 23.292$). The mean number of T4+ cells declined during HIV-Ab seroconversion and stabilized at a significant ($p < 0.05$) lower level in individuals seroconverting or seropositive for HIV-Ag than in individuals without HIV-Ag after HIV-Ab seroconversion. This indicates that low and declining numbers of T4+ cells may herald HIV-Ag seroconversion. The risk to develop AIDS and related disease appears to be strongly associated with persistent HIV antigenemia.

MP.54 Natural History of HIV Infections in Haemophiliacs

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The natural history of HIV infection continues to unfold and ongoing data is crucial. We have studied 48 HIV positive haemophiliacs. In 32 of these we were able to postulate the year of seroconversion through retrospective sampling. These were 1980 (1), 1981 (5), 1982 (10), 1983 (11) and 1984 (5). In the remaining 16 patients the year of seroconversion was no later than 1980 in 1, 1983 in 3, 1984 in 10 and 1985 in 2.

No case of AIDS has developed in our group. Seventeen (35%) have persistent generalised lymphadenopathy (PGL) and 7 (15%) are thrombocytopenic. PGL was first noted within the known year of seroconversion (year 0) in one patient, year 1 (1), year 2 (1), year 3 (3), and year 4 (3). The presence of PGL was not significantly correlated with time since seroconversion nor with T helper cell (T_4) levels, although 5 of the 9 patients with lowest T_4 levels had PGL.

T_4 levels were measured in 36 patients and were subnormal in 10 (28%). Seroconversion year was known in 21 of these and a significant negative correlation between time since seroconversion and T_4 levels was found ($r = .55$ $p = <.001$). The mean T_4 level in 9 patients who were known to have seroconverted more than 4 years previously was .91 x 10 9/L, while the mean level in 12 patients who had seroconverted less than 4 years previously was 1.8 x 10 9/L. The difference is highly significant ($p = <.001$).

In spite of the absence of AIDS so far in our patients, we believe that the progressive reduction in T_4 levels with time portends an ultimately high incidence of serious AIDS, although the incubation period appears to be longer than in other high risk groups.

MP.55 Continuing Surveillance of HIV Associated Morbidity and Mortality in a Well Defined Population

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In September 1985 we reported clinical and laboratory findings in 337 people in Northern England, including 143 multi-transfused haemophilic patients (Jones P, et al, AIDS and haemophilia: morbidity and mortalityin a well defined population, British Medical Journal 1985, 291, 695-9). Of 99 severely affected haemophiliacs 76 were anti-HIV seropositive; 3 of 36 female sexual partners then tested were also seropositive. At the time of publication 3 of 4 patients with AIDS had died. 15 months later a further 9 patients have developed AIDS; 4 are dead. One of these patients was the wife of a seropositive haemophiliac who developed pneumocystis carinii pneumonia and dementia. A further seropositive partner has given birth to a seropositive but clinically well child. The third seropositive female remains clinically well. 51 other female sexual partners have been tested and are seronegative; 41 had seropositive and 10 seronegative partners. Four of those presenting with AIDS had no clinical markers suggesting impending illness other than seropositivity at the initial survey; 2 presented with extra-cerebral lymphoma. A further patient with abdominal lymphoma is presently receiving treatment.

Whilst the prognosis for anti-HIV seropositive haemophiliacs remains uncertain these results suggest that AIDS may prove to be more common than earlier predictions for this population first indicated. Heterosexual transmission of HIV is less common than expected.

MP.56 Heterosexual Transmission of HIV in Switzerland

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Various sources are drawn on in Switzerland for the evaluation of the epidemiological situation. In addition to the case of AIDS reported, we also receive information on the persons who attend the anonymous test units or of blood donors whose HIV antibody tests show a positive result. Furthermore, all positive laboratory results are submitted in collective reports. The following results were obtained by end 1986.

Cases of AIDS: Of the 165 cases of AIDS in adults, 150 (=91 %) were men and 15 (=9 %) women. In the case of 6 of the Swiss men and 5 of the Swiss women, heterosexual transmission of HIV is reported as the sole risk situation.

Blood donors: Of the 52 cases of HIV antibody positive blood donors analyzed to date, 43 (=83 %) are male and 9 (=17 %) female. 5 (=12 %) of the men and 2 (=22 %) of the women reported heterosexual contacts as the sole risk situation.

Anonymous test: 335 of the men tested reported varied heterosexual contacts as sole risk situation. 4 (=1.2 %) of these were HIV antibody positive. Of the corresponding 178 women tested, 3 (=1.7 %) were HIV antibody positive.

Laboratory reports: Of the 4,268 HIV antibody positive reports, 3,111 (=73 %) are accounted for by men and 1,157 (=27 %) by women.

Summary: Heterosexual transmission of HIV can already be well documented today. The relevant measures to prevent increasing heterosexual transmission are imperative.

MP.57 HIV Antibodies in Seroconverters Followed by Weekly Intervals

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Sera from 26 patients were analysed for HIV-antibodies by five different methods. The patients were initially seronegative and became positive. The analyses were an indirect ELISA with HIV-antigen from H-9 cells (A), a commercial indirect ELISA, ELAVIA, with antigen from CEM cells (B), a commercial competition ELISA, Wellcozyme (C), a western blotting for HIV specific IgG (D), and a western blotting for specific IgG, IgA, and IgM antibodies (E). The first serum sample, which was positive by the screening test, (A), defined the day of seroconversion.

Sera from 10 different patients were collected within 1-4 weeks before seroconversion, where 4 were positive by (B) and 3 by (D) 1-2 weeks before (A). A singular reactivity on HIV-antigen p24 was observed for 6 patients by (D) and for 7 patients by (E) 1-3 weeks before (A).

Sera from 9 patients were collected 5-10 weeks before seroconversion. In this period 4 were positive by (B), 2 by (C), and 2 by (D) and (E), while they were borderline by (A). In the same period 3 sera were borderline by (A) and p24 reactive in (D). Only four sera showed borderline reactivity before this period.

Western blotting analyses were reactive earlier than the ELISA screening test. Some patients were clearly seropositive 1-2 weeks before they were identified by the ELISA screening method. These patients would escape the HIV antibody screening test.

MP.58 Absence of HIV infection in two sentinel cohorts of high-risk black South Africans.

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As at the end of 1986 no cases of AIDS had been recognised in black South African individuals; all 38 reported AIDS cases in South Africans have occurred in white males belonging to the high-risk groups characteristically seen in Western countries. To determine the possible introduction of HIV infection from African countries to the north, two cohorts of promiscuous African women, 56 black prostitutes "servicing" a large industrial complex north-east of Johannesburg and 195 black females attending the major Johannesburg clinic for sexually-transmitted diseases (STDs) were investigated for the presence of HIV infection. All sera were examined for HIV antibodies, both by ELISA (ELAVIA - Pasteur Institute) and by indirect immunofluorescence (IF) using HIV-infected H9 cells (obtained from Dr R Gallo).

None of the prostitutes and only one of the STD attendees were positive for HIV antibodies (both by ELISA and IF); the latter individual was, however, a migrant Malawian and not South African. Examination of these specimens for other STDs revealed prevalences consistent with those seen for similar populations elsewhere in Africa. In the prostitute cohort, 24 of 56 (43%) were HBsAg or anti-HBs positive and 53 of 56 (95%) were positive for chlamydia antibodies. Similarly, in the STD cohort, 81 of 195 (42%) were positive for HBsAg or anti-HBs, 27 of 108 (25%) were WR positive and 179 of 195 (92%) were positive for chlamydia antibodies.

There thus appears to be still no evidence of the spread and establishment of endemic African AIDS in South Africa.

MP.59 T-Lymphocyte Subsets in HIV Infected Drug Abusers and Long-Term Abstainers

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A study group of HIV infected IVDA, unique in 2 ways. Firstly, we have been able to pinpoint seroconversion dates, thereby excluding the possibility of different subgroups with different lengths of seropositivity. Secondly, the group comprises some long-term abstainers who are antibody positive, thus it has been possible to follow the clinical course of infection in both abstinent and current IVDA. In infected IVDA the presumption is often that continued use of drugs may increase the likelihood of progression to AIDS.

To determine the relationship of continued drug use to apparent disease progression, as measured by T_4/T_8 cell ratio, 10 abstinent and 10 current drug abusers had blood samples tested for T_4/T_8 ratio. Both groups had been seropositive for the same length of time.

Significant differences emerged in the ages of the two groups, the abstinent group being older ($p< .05$, 18 df). This group also had a significantly shorter length of heroin use ($p< .005$, 18 df). The T_4/T_8 cell counts were not significantly different.

These results suggest that no advantage is shown in those stopping heroin use, since in a comparable seropositive group abstinent from opiates (including methadone) T_4/T_8 ratios continued to be unfavourable. The provision of methadone for seropositive IVDA may be less appropriate than reducing the risks to those who remain seronegative.

MP.60 Early Indications of Unidirectional Heterosexual Transmission of AIDS in Botswana

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Botswana is situated south of the high prevalent regions of AIDS in Africa but has identified only 7 cases in the past 2 years.

Transmission is presumed to be predominantly heterosexual.

23 sexual partners of these cases have been followed and tested. 211 infectious diseases in-patients at 10 selected health facilities in the country were also screened for HIV infection.

The majority of cases (85.7%) are females who also constituted 61.5% of the positives among the health facility surveys. Approximately 62% of all known HIV infected individuals are females.

3 females who had evidence of HIV infection maintained one positive sexual partner each and at least another who remained uninfected over the period.

In early stages of AIDS in Botswana, it appears that males are more difficult to be infected than females who are therefore at a higher risk in a heterosexual relationship. This female preponderance is in excess of the sex distribution in the general population as well as the study population.

Differences in the anatomy and the physiology of the sexes and the varying doses of the Human immune deficiency virus in semen and cervical secretions have been given as some of the factors for this male to female transmission in Botswana.

Definitive conclusions must await further follow-up.

MP.61 HIV Infection in African Children with Sickle Cell Anemia

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To assess the importance of transfusions and injections in the transmission of HIV and to define the clinical spectrum of HIV infection in children with sickle cell anemia (SCA), we studied 241 children with SCA (aged 1-12 yrs; mean 6 years). We compared these patients (124 boys, 117 girls) with 126 non-sickle cell (NSCA) children (64 girls, 62 boys) of the same age. Thirteen SCA children were HIV(+) (5.4%) compared to 1 (0.8%) of the NSCA group. Seropositivity in the SCA group was associated with increased lifetime numbers of transfusions [mean 5.8 in HIV(+) patients(P) vs 3.4 in HIV(-)P] and the receipt of blood from paid donors (67% in HIV(+)P vs 52% in HIV(-)P) but not with the number of injections during the last 5 years (mean 76.5 in HIV(+)P vs 78.7 in HIV(-)P. Among SCA children HIV(+), patients were more likely than HIV(-) patients to present with failure to thrive (62% vs 21%, $p<.001$), polyadenopathy (62% vs 37%, $p<.05$), weight loss (38% vs 24%) or unexplained fever (23% vs 11%).

Transfusions in Africa appear to be a more important source of HIV infection in patients with sickle cell disease than injections. The pediatric spectrum of HIV infection in African sickle cell patients is similar to the one described in African children without sickle cell disease.

MP.62 Detection of HIV Antibodies in Whole Blood Impregnated Filter Paper Discs

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Eluation of HIV antibodies from whole blood impregnated filter paper (Whatman 3MM Chr) was performed by punching out a 14mm disc from the filter paper and eluating the antibodies in 2.5 ml PBS + 0.1% Tween 20 + 1% normal rabbit serum + 0.015 M NaN_3 for 2 hours at room temperature. This correspond to a serum dilution of approximately 1:100, and the eluate is tested in ELISA (undiluted) and immunoblotting (diluted 1:5). Corresponding serum and whole blood discs from 15 Danes and 16 East Africans were tested, as were serum discs and whole blood discs from 42 Central Africans.

A 100% correlation was found in both ELISA and immunoblotting by testing serum and whole blood discs from Danes and East Africans, of whom 5 and 3 were found HIV antibody positive, respectively. Likewise, testing of serum discs and whole blood discs from Central Africans, of whom 4 were antibody positive, revealed full agreement in both ELISA and immunoblotting. Whole blood eluates produced a slight but insignificant increase in OD values of the ELISA as compared to ordinary serum. No significant loss of antibody activity was observed neither in the eluates after storage for 3 months at $-20^{\circ}C$ nor in the filter paper discs after storage for 3 months at $+4^{\circ}C$. This technique may be useful to facilitate sample collection and transportation, particularly in remote areas of the world.

MP.63 The Sydney AIDS Project: Factors Associated with Progession to AIDS.

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In a prospective study of 996 homosexual men, 386 (38.8%) were HIV seropositive at enrolment. In 3 years, 32 of these seropositive men (8.3%) have developed AIDS. Compared with seronegative subjects, seropositives were more likely to have performed receptive or insertive anal or oral sex in the three months prior to enrolment. Immunologically, seropositives had a significant lower T4+ lymphocyte count and T4+:T8+ ratio and an increased T8+ lymphocyte count, compared with seronegatives.

Seropositives who developed AIDS reported greater use of marijuana in the previous 3 months than did seropositives who did not progress but the two groups did not differ on other lifestyle variables. Splenomegaly and hepatometaly were detected significantly more frequently as antecedent signs in subjects who developed AIDS. The absolute T4+ lymphocyte count was the most reliable antecedent indicator of development of AIDS. At enrolment (a median of 8.5 months prior to diagnosis) subjects who developed AIDS had a significantly lower T4+ lymphocyte count and T4+:T8+ ratio than did their non-progressing counterparts.

Overall these findings support the role of the established risk factors for the acquisition of HIV infection but have found no such co-factors for the development of AIDS. This study emphasises the value of a low T4+ count as the best measure of progression.

MP.64 Epidemiology of AIDS in Australia.

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Since the first case of AIDS was diagnosed in Australia in late 1982 there have been an additional 376 cases diagnosed including 14 women, of whom 200 have died. The majority, 88%, have been homosexual and bisexual men, but 27 or 7% have been transfusion associated, 13 of them women. To the end of 1986 there has been only one case resulting from intravenous drug usage, although an additional twelve were homosexual/bisexual men who also used intravenous drugs. Two cases have become infected as a result of heterosexual intercourse.

The initial diagnosis of AIDS was an opportunistic infection in 74% of cases and Kaposi's sarcoma in 18%. A further 3% were diagnosed with both opportunistic infection and Kaposi's sarcoma. Non-Hodgkin's lymphoma was the presenting disease in 5%.

A mathematical model based on a Poisson distribution was developed using the numbers of cases among homosexual and bisexual men from 1982-1986 to predict the future case load of AIDS. To those numbers, a constant figure of ten cases annually was added to account for those cases belonging to other groups. Using this model, we have predicted 500 new cases in 1988 and 1000 new cases in 1990. The cumulative total to the end of 1990 would be 3000 cases.

The epidemic of AIDS in Australia is following a similar pattern to that found in other western countries, with greatly increased numbers predicted in future years.

MP.65 Risk of AIDS after herpes zoster.

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All patients diagnosed with herpes zoster (N=112) between 1980 and mid-1986 in a closed internal medicine practice for homosexual men in Central Manhattan were evaluated with respect to time of eventual AIDS development or death. Using Kaplan-Meier survival analysis, 22.8% (+/-5.3%) developed AIDS within 2 years after herpes zoster, and 45.5% (+/-11.1%) after 4 years. The longest observation period was 6 years, at which an estimated 72.8% of the men had been diagnosed AIDS. Severity of the zoster (relative risk, RR =4.6), the degree of pain (RR=3.4), and zoster of the cranial or cervical dermatomes (RR=2.2) were all associated with a poor prognosis. Other clinical conditions which additionally increased the risk of AIDS included: oral thrush, oral hairy leukoplakia, amebiasis, and superficial (tinea) fungal infections. Oral thrush and oral hairy leukoplakia manifestations were diagnosed an average of 1.2 and 1.1 years, respectively, after the diagnosis of herpes zoster, making zoster an early indicator of an impaired immune system. Among hemophiliacs, the period between the development of human immunodeficiency virus (HIV) antibodies and zoster ranged from 21 months to 88 months, with a median estimate of 56 months. Adding the interval between HIV-seroconversion and zoster to the possible interval between zoster and AIDS, the risk of developing AIDS after HIV-seroconversion must continue at least 10-15 years.

MP.66 Cerebrospinal fluid abnormalities in homosexual/bisexual men with and without neuropsychiatric symptoms.

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A longitudinal study of the neuropsychiatric manifestations of human immunodeficiency virus (HIV) infection is underway within the MACS. 215 homosexual/bisexual men underwent neuropsychiatric screening in Baltimore. Cerebrospinal fluid (CSF) was obtained from 7 asymptomatic men who had become HIV-seropositive during 30 months of observation (ASC), and on 10 with neuropsychiatric symptoms, including 5 men seropositive > 30 months (SP), 5 seroconverters (SC).

CSF Findings	Symptomatic		Asymptomatic	Total
	SP (N=5)	SC (N=5)	ASC (N=7)	(N=17)
CSF pleocytosis (≥5 WBC/cu mm)	1 (20%)	3 (60%)	2 (29%)	6 (35%)
Oligoclonal bands (>1)	1 (20%)	3 (60%)	3 (43%)	7 (41%)
Elevated IgG index (>0.8)	0	0	3 (43%)	3 (18%)
Positive HIV culture	1 (20%)	0	1 (14%)	2 (12%)
Positive p24 antigen	0	1 (20%)	0	1 (6%)

CSF abnormalities are common in HIV-infected homosexual men, with or without neuropsychiatric symptoms. The most common finding was the presence of oligoclonal bands and a lymphocytic pleocytosis. The most striking finding was the incidence of abnormalities in asymptomatic seroconverters. Positive HIV culture and p24 antigen were rarely detected, and thus may be poor predictors for early brain involvement in HIV infection. Serial observations in larger numbers of homosexual men will be required to confirm this impression.

MP.67 A case of Acquired Immune Deficiency Syndrome without the Recognised Risk Factors

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Whilst the modes of transmission of HIV infection are now well established, it is important to retain a clinical awareness of the possibility of this infection in patients without apparent exposure to the recognized risk factors.

We report two cases of AIDS, apparently without the usual exposure factors, in whom a temporal association was detected after detailed epidemiological investigation.

The index case - a 45 yr old housewife, who developed Pneumocystis carinii pneumonia following a severe herpes zoster infection, and was shown to be anti-HIV positive. Three years prior to diagnosis she had been investigated for "glandular fever" and subsequent generalised lymphadenopathy, but no diagnosis was made. Detailed social history revealed no exposure to the relevant risk factors. However, three months prior to the onset of the "glandular fever", she had provided terminal home nursing care for a 33 yr old African man, who died from an undiagnosed encephalitis. At this time she had uncovered skin lesions on her hands. Review of post mortem pathology specimens allowed a retrospective diagnosis of AIDS with cerebral toxoplasmosis to be made for the African man.

The type of home nursing care given by index case, was quite different from that normally provided by health care workers with the training and facilities to prevent the spread of infection.

MP.68 Classification of HIV Infection in the Third World

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405 patients were referred to our AIDS clinic in Port-au-Prince, Haiti from July 1983 to June 1985 for diagnostic evaluations. HIV antibody (wv, p24, gp 120) was detected in 339 pts. (84%). Seropositive subjects were categorized based on their initial clinical evaluation and recategorized 1 yr. later. The signs and symptoms of patients in groups 2-5 were present for >1 month. Group 2 pts. had only prurigo. Group 4 had oral thrush alone (21) or with either tbc (18), S.enteritis (5) or H.zoster (4). Group 6 met CDC criteria. During a 1 yr. period 4/7 group 1 pts. developed thrush and 226/293 (77%) group 2-5 pts. died or met AIDS criteria. The 66 HIV seronegative pts. initially evaluated had other diagnoses (pul tbc, typhoid, malaria, giardiasis, etc). We conclude that wgt. loss with either fever or diarrhea is the most common presentation of AIDS and that prurigo is an early finding with a poor diagnosis. This classification defines the spectrum of HIV infection in Haiti.

Group	Number of Patients (%) Initial Evaluation		One Year Evaluation	
1 Asymptomatic	7	(2)	3	(1)
2 Prurigo	29	(9)	7	(2)
3 Adenopathy	7	(2)	1	(< 1)
4 Oral thrush	48	(14)	36	(11)
5 Weight loss and either fever or diarrhea	209	(62)	27	(8)
6 AIDS	39	(11)	211	(62)
7 Dead	--	--	54	(16)

MP.69 Kaposi's Sarcoma and AIDS in Haiti (1979-1986)

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We evaluated and treated 584 AIDS patients in Port-au-Prince, Haiti from June 1979 to December 1986. Kaposi's sarcoma (KS) was present in 53 patients (9%). The percentage of AIDS patients with KS has decreased from 15% (1979-83) to 5% (1985-86). KS lesions were the exclusive or predominant manifestation of AIDS in 32/53 (60%) patients, while the other 21 (40%) patients presented with opportunistic infections (OI). KS lesions were disseminated in 60% of cases with skin, lymph nodes, gastrointestinal tract and lungs as the common sites.

Male predominance was more marked for KS patients (92%) than for OI patients (72%). The annual percentage of female KS patients has been constant over time while the percentage of female OI patients increased from 14% to 28%. KS patients were comparable to those with OI in terms of age, socioeconomic status, place of residence and risk factors. 15% of KS males and 20% of OI males were bisexual, with other risk factors (blood transfusions, IV drug abuse) noted in 18% and 11%, respectively. Pruritic skin lesions (prurigo) were present in 23% of KS and 51% of OI patients. HIV antibody was detected in 96% of KS patients tested and also in 83% of their heterosexual sex partners.

Kaposi's sarcoma in Haiti is clearly associated with HIV infection, is decreasing in prevalence, and is not associated with any particular risk factors.

MP.70 Prospective Study of AIDS in Hemophiliacs with Elevated Interferon Alpha Levels

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We have previously shown that an acid labile form of alpha interferon (IFN) was persistently elevated in the sera of 3 hemophiliacs prior to the onset of AIDS. The prevalence and predictive value of serum IFN quantitated by a semimicrobiological assay (NEJM 1983: 309, 583-586) was assessed in 469 HIV seropositive and 346 seronegative hemophiliacs. Results at entry were as follows:

	IFN <8 IU	IFN ≥8 IU
HIV -	315	31 (9%)
HIV +	426	43 (10%)

Of the 43 HIV pos. IFN pos. (≥8 IU) hemophiliacs, 7 had AIDS and 11 developed AIDS within 16 months (42%). Four more (9%) had AIDS-related symptoms. Twenty-one (49%) have remained well up to two years. Four additional patients converted from IFN neg. to pos. prior to the development of AIDS during the study. In a subcohort of 84 hemophiliacs with HIV seroconversion dates, very high IFN levels (≥20 IU) predicted AIDS up to 1 year before diagnosis, even when controlled for duration of HIV infection ($p \leq .004$). In conclusion, the prevalence of IFN in HIV seropositive hemophiliacs was 10%. At least 42% (18/43) had AIDS (16%) or preAIDS (26%). Persistently elevated IFN, especially high levels, usually heralded the onset of AIDS in one year. The role of IFN in the pathogenesis of AIDS has not yet been determined. However, its predictive value may be complementary to quantitation of T cell subsets.

MP.71 Human Immunodeficiency Virus (HIV) Infection in Spouses of HIV Seropositive Active Duty Navy and Marine Corps Personnel

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The United States Navy is conducting a Navy-wide HIV screening program of all active duty personnel. All personnel found to be HIV seropositive are referred to one of four major evaluation centers. To date, 324 HIV positive active duty personnel have been evaluated at Naval Hospital Portsmouth. Thirty-three percent of these individuals are married. Evaluation of these dependent spouses was offered to all HIV seropositive personnel. No spouse in the immediate geographic area refused evaluation. Thirty-four spouses have been evaluated. Ninety-four percent (32/34) were female; 6% (2/34) were male. Mean age of evaluated spouses was 27 years with a range from 16-42 yrs. Forty-four percent (15/34) were white, 41% (14/34) were black, 9% (3/34) were Oriental, and 6% (2/34) were Hispanic. Risk factors for HIV infection in spouses included being the steady sexual partner of an HIV positive spouse (85%), being the recipient of multiple blood transfusions (9%), and being bisexual (3%). Thirty-five percent (12/34) of all spouses evaluated were HIV seropositive. Among spouses where the only risk factor was an HIV seropositive spouse, the seropositivity rate was 29% (8/28). Among 32 female spouses evaluated, three (9%) had AIDS or ARC. Nineteen percent (6) of female spouses were pregnant at the time of evaluation. One pregnant woman was HIV seropositive. Two HIV seropositive children have been detected.

Dependent spouses of HIV seropositive active duty personnel are at significant risk for acquisition of HIV infection. This population is young, female, and actively engaged in child bearing. Evaluation and counseling for spouses and children are essential to any large-scale HIV infection screening program.

MP.72 Serologic Evidence for Infection by HIV-2 in Guinea Bissau in 1980.

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Human immunodeficiency virus type 2 (HIV-2, originally called LAV-2) was recently isolated from AIDS patients from the West African countries of Cape Verde and Guinea Bissau. HIV-2 is more closely related to the simian immunodeficiency viruses (SIV) than to HIV-1 both serologically and by nucleic acid hybridization. To determine the past prevalence of HIV-2 in some areas of West Africa, we tested 440 serum samples collected in Guinea Bissau in 1980. The samples originally were collected to test for the prevalence of antibodies to Lassa virus in adults living in rural areas. We first screened the serum for antibodies to an HIV-like virus by ELISA using purified SIV_{mac} as antigen. A large proportion (30%) gave OD readings greater than 0.5, which was peculiar to human serum because a large number of monkey serum (195 of 214) from Africa gave OD readings less than 0.2 in the same SIV_{mac} ELISA. All of the human samples with OD readings greater than 0.9 (28) were tested by immunoblot and immunofluorescence assays for antibodies to SIV/SMM, HIV-2, and HIV-1. Five human serum samples were repeatedly reactive by all assays to both HIV-2 and SIV/SMM. Antibodies to gag, env, and pol gene products of HIV-2 and SIV/SMM were detected on immunoblots. Five of 440 human sera were positive for antibodies to HIV-1 using the Abbott HTLV-III EIA kit, but none could be confirmed as true positives by immunofluorescence and immunoblot assays. Thus, in 1980, 1.1% (5 of 440) of a random sample of persons in Guinea Bissau had been exposed to a virus highly related to HIV-2 and SIV/SMM, but there was no evidence of infection by HIV-1.

MP.73 Absence of Association between HIV Seropositivity and Plasmodium falciparum Malaria in Kinshasa, Zaire.

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Because Plasmodium falciparum malaria and HIV infection coexist in several areas of Africa, the relationship between these two entities was investigated at the Mama Yemo Hospital (MYH) in Kinshasa, Zaire, between July and December 1986. Among 333 children evaluated at MYH, the HIV seropositivity rate in children with P. falciparum malaria (1.2%) was not significantly different from that in asymptomatic, healthy children (0.6%). Among 1046 children presenting at MYH for various medical complaints, no significant difference was detected between the HIV seropositivity rates in 540 children infected with P. falciparum (2.8%) and in 506 uninfected children (4.9%). Among 1156 healthy adult MYH employees, a malaria slide positivity rate of 6.2% and an HIV seropositivity rate of 6.0% were found, with no association detected between these two variables. In an ongoing study in pregnant women delivering at MYH, the first 195 patients had a P. falciparum infection rate of 19% and an HIV seropositivity rate of 7.2%, with no association detectable. This overall absence of association indicates that P. falciparum does not act as an important opportunistic agent in individuals infected with HIV in Kinshasa.

MP.74 Analysis of the AIDS epidemic in The Netherlands in comparison with data from the San Francisco CDC study cohort

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Using data from The Netherlands and the San Francisco CDC study cohort Mathematical models were formulated to estimate a) the annual effective contact rate i.e. the average number of sexual contacts per person per year that results in transmission of HIV and b) the number of homosexual men already infected from the cumulative number of persons with AIDS.

If there is a delay of 3 years, 20,000 homosexual are assumd to be at risk in The Netherlands in the initial stage of the epidemic and the annual effective contact rate is estimated to have a value between 1.0 and 1.2. The width of the interval depends on the initial growth rate of the epidemic and the average duration of the infectious period in persons infected with HIV. The results indicate that the probability of transmission of HIV per sexual contact is low. Given 200 homosexuals with full blown AIDS in The Netherlands, the number already infected adopts a value between 5,000 and 15,000.

The models were also used to predict the long term course of the epidemic. The results indicate that in the absence of prevention HIV infection will become endemic in high risk homosexual communities with a prevalence larger than 70%. Furthermore an efficacy of e.g. 50% in the reduction of the annual effective contact rate probably has a limited effect; one should aim at a 90% efficacy (or more).

The mathematical models and the simulation approach are helpful in predicting the impact of intervention measures.

MP.75 Exposure to the AIDS virus through artificial insemination in a population of lesbians in California.

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In 1985, Australian investigators reported that four women who were artificially inseminated tested positive for the AIDS antibody. All four women had received semen from the same donor who was later found to be antibody positive. None of the women had any other risk factors for AIDS. The purpose of the present investigation is to examine in a more comprehensive study the transmission of the AIDS virus through artificial insemination. We have chosen to study transmission in lesbian women because lesbians do not, as a rule, engage in heterosexual intercourse and therefore, we could eliminate the contribution of specific sexual practices. In addition, lesbians often select gay men as donors and the incidence of AIDS among the gay population of California is very high.

In a pilot study of 48 lesbians in San Francisco, we found that all tested negative for antibody to the AIDS virus. This study was expanded to include lesbians across the state. Each woman who agrees to participate is tested for antibody to the AIDS virus and completes a questionnaire designed to elicit information about her donor insemination history (vaginal vs intrauterine insemination, fresh vs frozen semen, antibody status of donor, health status and sexual orientation of the donor, etc.) and her sexual, health, and reproductive history. As of January 1987, 20 lesbians have participated. These women reported obtaining semen from 14 homosexual, 10 heterosexual, and 3 bisexual donors (5 addtional donors were of unknown orientation). One homosexual donor has a known positive antibody status and another died of AIDS a year after donating semen. To date, all women have been seronegative. We will report on an update of this study.

MP.76 Low Risk of Anti-HIV Seroconversion in Female Sexual Partners of Haemophiliacs and their Children.

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The objectives of this study were to quantitate risks of HIV transmission from haemophiliacs to their sexual partners and children; and to identify risk factors for such transmission. A detailed questionnaire was used to assess frequency and modes of sexual contact, contraceptive practice, and other risk factors. The presence of anti-HIV, measured by a competitive ELISA assay, was used as a marker of exposure to the virus. 100 contacts were studied. Contacts of 45 seropositive patients (median period of seropositivity 3 yrs., range 3 mo - 6 yrs) comprised: 30 regular female sexual partners; 21 parents giving clotting factor concentrates to their children; and 10 children aged less than 10 yrs of haemophilic fathers. Contacts of the 28 seronegative patients were similarly distributed. Only one contact was found to be seropositive, giving a 3.3% prevalence rate in the sexual partners of seropositive patients. Risk factor analysis showed nothing to distinguish this couple from other members of the group except that both were abusers of i.v. heroin. Subsequently, however, the man died from zoster pneumonia, the only patient in the study to die from possible HIV related illness. At the time the study started, when all the index patients but few of their sexual partners had been formally counselled, only 23% of the 'seropositive' couples regularly used barrier methods of contraception, compared with 7% in the seropositive group. Following repeated counselling of both partners, the proportion using barrier methods increased, but still remained a minority. All 5 children who must have been conceived at a time when their fathers were seropositive remain well and anti-HIV seronegative.

MP.77 Relationship between P.falciparum malaria and HIV seropositivity at Ndola, Zambia.

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One hundred and seventy-two patients presented with symptoms suggestive of malaria in January 1987, at the height of the transmission season. Patients were screened for (i) anti-HIV using the Wellcozyme test, (ii) malaria parasitaemia, and (iii) specific antibodies against P.falciparum using immunofluorescence (IFA) test, significant titres being defined as 1:80 or greater. Two patients with P.malariae have been excluded from analysis.

Sixty-seven (39%) of the patients had P.falciparum and 28 (16%) were anti-HIV positive. Of the 103 patients without malaria, 20 (19%) were anti-HIV positive compared to only 8 (12%) of those with malaria ($X^2 = 1.15$, $p = 0.28$).

Sixty-three (94%) of the patients with parasitaemia and 74 (72%) of those without parasitaemia had significant IFA titre. No significant relationships were found in the parasite positive or parasite negative groups between antimalarial IFA and anti-HIV.

These data do not support the hypothesis that HIV infection increases the risk of clinical P.falciparum malaria.

MP.78 Transmission of Human Immunodeficiency Virus from Hemophiliacs to their Sexual Partners: Role of Parenteral Exposures

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To evaluate the risk of transmission of human immunodeficiency virus (HIV) from hemophiliacs to their female sexual partners (SP), 31 infected hemophiliacs and their SP were studied. One man with 2 SP was counted as two separate couples. HIV infection determined by Western blotting and/or virus isolation was detected in 5 SP (15.6%) of 32 HIV-infected hemophiliacs. Three of the 32 hemophiliacs were intravenous drug abusers (IVDA). The 2 SP of 2 hemophiliac IVDA had HIV infection (100%), whereas the third couple, which included a nonIVDA sexual partner, showed no HIV transmission. Confidential, coded questionnaires were administered to 18 HIV-infected hemophiliacs and their SP. Parameters examined included history of needlestick injuries while the SP assisted in clotting factor treatments, receipt of any transfusions by the SP, intravenous drug abuse, condom usage, oral or anal sex, history of vaginal infections, and monthly frequency of intercourse (since 1981). This cohort excluded any IVDA. Of the 18 SP at risk, there was HIV transmission to three (15%). Two of these couples reported no use of condoms. However, the couple which did use condoms regularly reported 8 needlestick injuries. Seven of the 15 uninfected sexual partners of HIV-infected hemophiliacs reported no usage of condoms. There was one reported needlestick injury in one SP in this group. In addition to heterosexual transmission, these data indicate that parenteral exposures are a potentially important risk factor among SP of HIV-infected hemophiliacs. Also shown is the inconsistent use of barrier contraceptives among couples at risk for heterosexual transmission of HIV.

MP.79 HIV1 and HIV2 infection in a french cohort of homosexual men, in Paris.

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A cohort has been composed in order to analyse several risks factors in sexual practices among homosexual men in Paris (France). All subjects are consultants of general practitioners and are asymptomatic. They will be followed up for a minimum of three years on clinical, immunological and virological parameters. We present virological results on the first hundred included subjects. The sera were tested by ELISA HIV1 and HIV2 (Diagnostics PASTEUR) (DP). All positive results were confirmed by Western Blot analysis HIV1 and HIV2 (DP) : 34 % sera were strongly positive for HIV1, 1 % sera were positive for HIV2 (confirmed by RIPA-HIV2 (Pr. MONTAGNIER)). This subject is malian and has been living in France for ten years. An interesting point is the revelation of only 6 ELISA HIV2 positive sera among the 34 HIV1 positive sera (this raised the question of peculiar cross reaction, or double infection or eventually intermediary virus).

Moreover, the detection of HIV1 antigen has been performed by antigen-capture (DP). Only two patients are strongly HIV1 antigen positive (both of them are AB HIV1 positive). The specificity of these two positive results has been confirmed by neutralising reactions. The two subjects are asymptomatic so far and their follow-up will be informative. These two sera were also positive with HIV1 Ag test from A88OTT Lab.

These preliminary results show a low prevalence of HIV2 infection compared to HIV1 but raise the question of the spreading of HIV2 among homosexual men in Paris.

MP.80 Seroepidemiologic evidence of HIV2 infection in Mali and other West African countries and of its heterosexual transmission.

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HIV2 has been isolated recently from AIDS patients and healthy subjects from West Africa. It differs from HIV1 by antigenicity and molecular sequences.

Sera from 9 patients hospitalized in Bamako for "slim disease" were screened for HIV1 and HIV2 antibodies (Ab) by indirect immunofluorescence (IF) and radioimmunoprecipitation assays (RIPA). One patient, a zairian, was positive for both HIV1 and HIV2, and 3 for HIV2. One of the latter was hospitalized subsequently in Paris presenting with major weight loss, chronic diarrhea, esophageal candidiasis and infection with several opportunistic intestinal pathogens; he died a few months later. A study of 43 family members revealed that his wife was healthy but seropositive for HIV2, suggesting that HIV2 can be transmitted heterosexually. A stepmother was also Ab-positive but all other family members including his 3 children were Ab-negative.

This evidence of HIV2 infection in Mali prompted a wider study to determine the prevalence of Ab to HIV1 and HIV2 in 600 sera selected randomly from West African students living in Paris. All sera were screened by IF ; equivocal results were confirmed by RIPA. To date, screening of 100 sera obtained in 1984 revealed no Ab ; among 100 sera from 1986, one male was positive for HIV1 and another for HIV2.

The complete results of these serologic studies will be presented.

MP.81 Surveillance of Geographic Spread of HIV Infection

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The U.S. HIV epidemic began in a few circumscribed urban centers. We examined the first year of data from screening civilian applicants to U.S. military service to determine geographic spread of infection. A "geographically weighted prevalence" (GWP) was calculated for each county (a function of its first six months' crude county prevalence (CCP) and those of contiguous counties). We hypothesized that the GWP would predict subsequent county prevalences better than prior CCP alone, if county prevalences are influenced by their neighbors' prevalence. To test this hypothesis, we examined a subset of 48 eastern U.S. counties. Data from these counties revealed the following: For black applicants, the first six months' CCP vs. second six months' CCP, correlation=0.10 (p=.50); GWP vs. second six months' CCP, correlation=0.41 (p=.005). For white applicants, the first six months' CCP vs. second six months' CCP, correlation=0.20 (p=.17); GWP vs. second six months' CCP, correlation=0.34 (p=.02). The hypothesis of geographic spread from high prevalence areas into low prevalence areas is supported strongly for the black applicant population, but less convincingly for the white applicant population. Maps of the eastern U.S. displaying CCPs for the first, second and third six month periods, and GWPs, reinforce statistical criteria on which the conclusions are based.

MP.82 Transmission of HIV to partners of Seropositive Heterosexuals from Africa.

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Heterosexual transmission of HIV among individuals originating from or having resided for prolonged period of time in Africa was evaluated.

Thirty-eight spouses and/or regular partners of 35 HIV-seropositive heterosexual males (18 Afr.,17 Eur.) and 10 spouses and/or regular partners of 10 HIV-seropositive heterosexual females (9 Afr.,1 Eur.) were tested for HIV-antibodies using ELISA and IF or Western-blot methods.

All the spouses and partners had their medical history including sex life habits recorded and had a physical examination.

Overall seropositivity among the female partners was 73% (28/38) and 40% (4/10) among the male partners.

HIV cultures carried out in 7 male and 6 female seronegative partners were positive in 3 and 2 respectively.

Overall HIV infection rate was thus 81% among the female partners and 60% among the male partners. Of the female partners, 3 had a history of promiscuous heterosexual activity, 6 had $\leq$ than 5 partners, and 29 were monogamous with no other risk than heterosexual activity. Evidence for female to male transmission was obtained by primoinfection in 2 cases, monogamy in 1 case and by positive HIV culture in a seronegative male who had recent sexual contacts with a seropositive female.

Our data suggest that to be the spouse or the regular partner of an infected heterosexual individual is a major risk factor for acquiring HIV infection. HIV transmission rate in this study was significantly higher than rates found in the group of heterosexual hemophiliacs and transfusion recipients.

MP.83 HIV Infection in Sexually Active Heterosexual Adults Attending a New York City STD Clinic.

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To evaluate heterosexual transmission of HIV among sexually active persons, patients attending a sexually transmitted disease (STD) clinic in New York City were enrolled in an ongoing case-control study that included serologic testing for HIV antibody, hepatitis B, and syphilis and an interview about sexual practices and known risk factors for HIV infection. From December 1, 1986, through January 21, 1987, 64 men and 25 women were enrolled (72% black, 13% Hispanic and 12% white; median age = 27 yrs; current enrollment = 60-80 patients/month). Antibody to HIV was present in 2 of 4 homosexual men, 5 of 11 bisexual men, and 6 of 9 heterosexual intravenous drug abusers (IVDA). None of 65 heterosexual non-IVDA had HIV antibody, including 10 persons (5 women and 5 men) who had sexual contact with an IVDA. The remaining 55 heterosexual non-IVDA had a median of 15 different sexual partners since 1978; 41 (75%) had a history of at least 1 previous STD, 16 (29%) had engaged in rectal intercourse, 36 (65%) never or rarely used condoms, and 15/38 (39%) men reported sexual contact with a female prostitute. In the city with the largest number of heterosexual AIDS patients in the United States, these preliminary results suggest a low prevalence of HIV infection among sexually active heterosexual adults who are not IVDA.

MP.84 Human Immunodeficiency Virus Infection in Patients with Hepatitis B. Virus and Hepatitis Delta Virus Infections in Los Angeles, 1977-1985.

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Stored sera from 723 patients with acute and 228 with chronic hepatitis B seen in Los Angeles between 1977 and 1985 were tested for antibody to human immunodeficiency virus (anti-HIV). We first detected anti-HIV in homosexual men in 1979 and in intravenous (iv) drug users in 1981. For acute hepatitis B, the seroprevalence of anti-HIV in homosexuals ranged from 14-33%, with no significant change from 1980-1985; seroprevalence rates in heterosexuals, including iv drug users, remained under 5%. Age stratified prevalence rates were higher in homosexuals and iv drug users with chronic than with acute hepatitis, and in homosexuals compared to non-homosexual subjects. In chronic hepatitis B, anti-HIV seroprevalence reached 50% in homosexual men in 1983 and 30% in iv drug users in 1985. A significant association existed between infection with HIV and hepatitis delta virus in homosexual men but not in iv drug users. Anti-HIV seroconversion rates in homosexuals with chronic hepatitis B were 22% in 1983 and 8% in 1985. Increased frequency of HIV infection in chronic hepatitis B probably reflects more extensive exposure. Our findings suggest that HIV transmission has reduced in recent years in homosexual men, in whom delta hepatitis and HIV infection share common risk factors.

MP.85 HIV Screening in the High Risk Obstetric Population and Infant Serologic Analysis

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Voluntary screening by a commercially available Enzyme Linked Immunoabsorbant Assay (ELISA) for seropositivity to Human Immunodeficiency Virus (HIV) was conducted in an inner city obstetric population over a six month period. Of one hundred fifteen women who identified themselves to be at risk for HIV infection and consented to testing, thirty-four, i.e., 29%, were confirmed seropositive. Most of the women (90%) had used intravenous drugs, the remainder were sexual partners of IV drug users.

Ten children born to these women have been followed for six months or greater. Of these, five children can be demonstrated to be endogenous seropositives: Western Blot analysis revealed two children who developed IgM against gp41 or p55 by 4 months of age and one child who developed new IgG bands against p55 and p66 at three months of age. Standard ELISA testing documented two children who lost and then reacquired seropositivity by nine months of age.

Three of the five children with serologic evidence of infection have clinical disease: one has marked lymphadenopathy, one has AIDS Related Complex and one has AIDS. The two children who developed IgM against HIV show no symptoms.

Neonatal serologic analysis of antibody to HIV has allowed identification of those infants producing endogenous antibody, thereby permitting earlier diagnosis and treatment of infected children. These results support earlier evidence for approximately 50% perinatal transmission rate. The possibility that early IgM synthesis against HIV may reduce the development of clinical disease is suggested.

MP.86 Natural History of Immune Function in HIV Infected Hemophiliacs.

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As part of a prospective study of immune function following human immunodeficiency virus (HIV) infection in hemophiliacs, 93 hemophiliacs (9 seronegative, 11 seroconverters and 72 seropositive) have been followed over a 4 year period.

MEAN DATA FROM 4 YEAR OF STUDY SEROPOSITIVE AND SERONEGATIVE HEMOPHILIACS

		Year 1		Year 2		Year 3		Year 4	
	N	T helper*	PWM**	T helper	PWM	T helper	PWM	T helper	PWM
Normal Controls	30	928	100	995	100	972	100	1010	100
Seronegatives	9	1228	78	1141	88	1065	72	1062	88
Seroconverters	11	954	82	849	54	670	24	415	45
Seropositives	72	740	45	727	44	589	40	519	38

*=cells/ul; **=%control counts per minute

Seroconversion in 11 of 93 occurred between year 1 and 2 of the study. HIV infected individuals have shown a progressive decline in T helper cell numbers and function as measured by pokeweed mitogen stimulation. Recent seroconversion (within 2 years) following HIV infection is associated with significant ($p<.05$) loss of T helper cells. One-third (33%) of our total seropositive hemophiliac population has shown progressive decline of T helper cells to 400/ul or less during a maximal exposure period of 4-7 years. These data strongly support a high rate of progressive immunologic attrition in HIV infected hemophiliacs.

MP.87 Serum HIV Antigen (HIV-Ag) as a Predictor of Progression to AIDS and ARC in Homosexual Men

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To test the presence of serum HIV-Ag as a predictor of subsequent disease, we studied 30 initially healthy anti-HIV seropositive homosexual men undergoing prospective study for two years. Ten subjects had less than 400/mm3 T-helper cells at entry or at followup (Group 1). Ten subjects had greater than 600/mm3 T-helper cells at baseline and at followup (Group 2); and ten subjects had less than 600/mm3 T-helper cells at baseline but had a net gain of 200 T-helper cells at followup (Group 3). HIV-Ag was detected in sera using the Abbott sandwich enzyme immunoassay for HIV p24. HIV-Ag was present in 6 subjects, all in Group 1. 6 of 6 HIV-Ag positive subjects developed ARC and 4 subsequently developed AIDS. 1 subject (from Group 3) of 24 HIV-Ag negative subjects developed ARC ($p<0.0001$). The remaining 23 subjects remained healthy for the entire period of the study. 4 of the 6 with Ag positive specimens were positive at baseline and followup (3 AIDS, 1 ARC); 1 at baseline only (AIDS); and 1 at followup only (ARC). The 4 subjects developing AIDS were diagnosed from 26 to 32 months after the first HIV-Ag positive serum specimen. The presence of HIV antigen in serum, as detected by this assay, is highly predictive of development of ARC or AIDS, and may be detected up to 32 months prior to progression.

Supported by a grant from the Universitywide Task Force on AIDS.

MP.88 Association of Donor Characteristics with Transmission of HIV Infection to Recipients

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By testing sera stored prior to the availability of routine anti-HIV screening, a national, multicenter study has identified 91 recipients transfused with anti-HIV(+) components. Among these 81 (89%) are anti-HIV(+) and 10 (11%) are anti-HIV(-). In 15 instances, 2 recipients in the study received blood from the same donor. In 13 pairs, both recipients are anti-HIV(+). In 1 case, one of the recipients became anti-HIV(+) and the other is anti-HIV(-); the donor was a 19 yr. old male. In the last pair, both recipients are anti-HIV(-); the donor was a 26 yr. old bisexual male.

In comparing characteristics of donors who transmitted infection (Group I) to those who did not (Group II), similar sex and age distributions were seen. Groups I and II also had similar mean enzyme immunoassay (EIA) absorbances (0.99 vs 1.16, NS) and ranges. Group II had higher percentages with P150 (29% vs. 5%, p=.10) and P120 (43% vs. 17%, p=.12) on immunoblot (IB). All donors had GP41 and P25 on radioimmunoprecipitation (RIP) and P24 on IB, and all but 3 donors in Group I had P41 on IB. A somewhat greater percent of Group I donors came from a high AIDS risk area (53% vs 29%, NS). Among 25 Group I and 5 Group II donors enrolled for further followup, 79% and 60% respectively are homosexual or bisexual males. 93% of the Group I donors are free from clinical signs of AIDS 1-2 yrs. post-donation, although 63% have T4/T8 ratios < 1. Thus, no clear relationship between the characteristics of the donor and transmission of HIV infection to the recipient can be seen. (Supported by Contract Nos. NO1-HB-4-7002 and NO1-HB-4-7003 of the National Heart, Lung and Blood Institute.)

MP.89 HIV Transmission Among Homosexual Male Partners: Evidence of the Inefficiency of Transmission.

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To evaluate the rates of transmission of HIV among homosexual couples, we studied 158 sexual partners of people with AIDS, ARC and HIV seropositive and seronegative healthy men. HIV seropositivity rates for partners of AIDS were 62% (16/26), partners of ARC were 40% (13/34), partners of healthy seropositive were 45% (13/29), and partners of healthy seronegatives were 20% (14/69).

Of the 158 pairs, 63 (40%) were concordant seronegatives, 42 were concordant seropositives (27%), and 53 (33%) were discordant. Virus isolations were attempted on each partner of the discordant pairs, and an isolation rate of 0% among the negative partners and 21% among the positive partners was found.

None of the 36 discordant pairs that have returned for their six month follow-up visit have become infected. This is of interest because 27 (75%) of the seronegative partners had engaged in unprotected sexual activities ((28% receptive anal), (72% receptive oral)) with their infected partner during this time period. These results indicate that there may be additional nonbehavioral factors related to HIV transmission and susceptability.

MP.90 Prospective Immunologic Study of Intravenous Drug Abusers (IVDA) Enrolled in a Methadone Program.

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173 patients with IVDA had baseline evaluations from September, 1984 to April, 1986 in a study designed to examine parameters associated with serum antibody to HIV and predictive of conversion to ARC and AIDS.

53 patients or 31% had antibodies to HIV by ELISA with confirmation by Western Blot, performed by C.W. Saxinger and S.H. Weiss at the NCI. The following mean laboratory parameters were statistically different ($p < 0.01$) between HIV-negative and -positive patients: (1) CDT_4/CDT_8 ratio, 1.50 vs. 0.90, (2) C1q 30.2 vs. 56.5 ug/ml, (3) beta-2 M, 2595 vs. 3363 ug/l, (4) absolute lymphocyte count 2578 vs. 1856/cmm, (5) % CDT_4, 34 vs. 27, (6) absolute T_4 894 vs. 492/cmm, (7) % CDT_8 25 vs. 33, (8) absolute T_3 1436 vs. 1014/cmm, respectively. Total interferon titers ($p < 0.05$) of negative vs. positive mean values were 1:8.8 vs. 1:23.

None of the 53 HIV-positive patients had AIDS on initial evaluation but 16 (30%) had LAS. In the HIV-positive subjects, beta-2 M was increased above 2500 in 37, and the absolute T_4 count below 500 in 30. Interferon level was elevated above 1:16 in 9. During the subsequent year, 5 patients developed AIDS and a 6th developed severe recurrent bacterial pneumonias. All 6 of these subjects were characterized by elevated beta-2 M (mean 4259) interferon (mean 107) and low absolute T_4 counts (mean 203).

In this cohort of HIV positive subjects, 9.4% prospectively developed AIDS within 1 year. All had elevated beta-2M and interferon levels and absolute T_4 count averaging 203/cmm.

MP.91 Female to male heterosexual transmission of HIV infection in Nairobi

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HIV is apparently transmitted with greater ease via heterosexual intercourse in Africa than in other regions. Concomitant STD's particularly genital ulcer disease (GUD) has been postulated as one co-factor which might facilitate sexual transmission. In order to quantitate the risk of HIV acquisition by a man after a single exposure to an infected woman and to determine if GUD increased the risk of HIV transmission we are conducting a prospective study of men who acquire an STD from a group of prostitutes with a known high prevalence of HIV infection (>85 %, HIV+). All men presenting to our clinic with an STD who reported one of these prostitutes as a source contact were enrolled in the study. 277 men have been enrolled in the study of which 9 % were initially HIV+. The major risk factor for HIV+ was a past history of GUD. Number of lifetime sex partners, frequency of prostitute contact, number of injections, blood transfusions and a past history of urethritis did not correlate with HIV+. 130 seronegative men have been followed for a mean of over two months. Seroconversion to HIV occurred in 6/54 men with chancroid, 3/69 men with urethritis and 0/7 men with other diagnoses (p = NS). Overall HIV seroconversion has occurred in 9/130 or 7 % of exposed men. The risk of HIV transmission from an HIV-infected prostitute to a male sex partner is substantial and may be facilitated by GUD.

MP.92 Relationships Between Decline in CD4 Lymphocytes and Other Variables Among 1828 Seropositive Gay Men.

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Longitudinal data were available at 4 visits six months apart. In order to relate the decline in CD4 cells to changes in other variables over time and to levels of variables available only at entry, we used an autoregressive model in which one relates CD4 cell number to covariates, conditioning on previous number of CD4 cells.

In the final multivariate model, the following variables were significant predictors of subsequent number of CD4 cells after controlling for previous number of CD4 cells: CD8 cells, platelets, serum IgA, hemoglobin and HIV antibody level. To measure the magnitude of the predictive power of these significant variables, we compared the subsequent numbers of CD4 cells of two individuals who differed by approximately one standard deviation in a given covariate but were identical otherwise (including the prior number of CD4 cells). The percentage reductions of CD4 cells associated with differences in a given covariate were as follows:

% fewer CD4 cells	Difference in covariate
7.8%	1.5 times the number of CD8 cells
3.7%	decrement of 50,000 platelets
1.7%	decrement of 1.0 gm% of hemoglobin
1.4%	2.0 times the IgA level
1.4%	decrement of 0.5 in OD of HIV antibody

These data suggest that several covariates in addition to previous number of CD4 cells have significant predictive power for estimating the decline in CD4 cells in HIV seropositive subjects.

MP.93 HIV-seroconversion in a Cohort of Homosexual Men in Stockholm between 1983 and 1986.

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Since Nov 1982, a clinic in Stockholm with gay staff has offered healthy gay men venereological screening. A consecutive serie of 166 men who first attended in Feb-May 1983 has been followed at yearly intervals. Examinations included HIV-serology, T-lymphocyte subsets and serum-electrophoresis.

Results: In 1983 HIV-antibodies were found in 31/166 (18.7%). In 1984 10 (8.0%) of the 125 previously negative men who returned had seroconverted. A further 4 (4.0%) had seroconverted in 1985 when 101 previously negative men returned, and of the 85 previously negative men who returned in 1986 5 (5.9%) had seroconverted. The T-lymphocyte subsets and IgG levels before (0) and at the first (1), second (2) and third (3) year after seroconversion were as follows:

	0	1	2	3
T4 ($x10^9/l$)	0.97 ± 0.38	0.69 ± 0.27	0.60 ± 0.24	0.59 ± 0.26
T8 ($x10^9/l$)	0.81 ± 0.42	1.00 ± 0.49	0.88 ± 0.37	0.79 ± 0.22
T4:T8	1.3 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2
IgG (g/l)	11.7 ± 2.3	12.9 ± 2.6	13.9 ± 2.7	14.0 ± 1.5

Conclusion: HIV-seroconversion is still seen in this prospectively followed co-hort in spite of decreasing risk factors. The implications of this will be discussed. Early after seroconversion there was a fall to a persistent low level of T4 lymphocytes and a transitory increase in T8 lymphocytes. IgG increased progressively during the follow up.

MP.94 Reactivity of Ghanaian Sera to Human Immunodeficiency Virus (HIV) and Simian T-Lymphotropic Virus III (STLV-III).

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Acquired immunodeficiency syndrome (AIDS) in Africa which was previously confined to the East and Central African countries is now in West Africa. The disease in Africa may take an epidemic character if measures are not taken to check its spread. Prevalence rates and the risk groups therefore need to be assessed and identified. Detection of antibodies (Abs.) to HIV and STLV-III antigens (Ags.) was carried out in human sera from blood donors, prostitutes, sickle cell disease patients and others. The ELISA and Immunofluorescence (IF) techniques were used for HIV Ags. and IF for STLV-III.

Out of a total of 997 samples (226 from prostitutes) examined for HIV and 737 for STLV-III. Abs. 93 including 57 prostitutes were positive for HIV and 18 for STLV-III Abs. Some of the sera reacted better to STLV-III Ags. Western blotting test also confirmed these differences.

Reports on Senegalese showed that some reacted to STLV-III Ags. Without any disease. The Ghanaians reacting to STLV-III showed disease. The Western blotting reaction suggests that some of the Ghanaians have been exposed to a virus which may be closely related to STLV-III.

A new virus HTLV-IV has been reported from Senegal. Retrovirus infection in Africa may therefore be more varied than in the Western Hemisphere. Isolation and characterization of local strains of HIV and their inclusion in tests as Ags. may be necessary to determine the incidence rates in some of these African countries. Work is currently going on in this direction.

MP.95 Concomitant HTLV-I and HTLV-III Infections - A Serological Survey in Washington, D. C. Area

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A serological survey for the presence of antibody against HTLV-I and HTLV-III (HIV) was conducted on serum samples collected in 1984 from four groups of individuals: (A) VDRL (-) premarital individuals (n=113), (B) senile, chronic disease patients in D. C. Village Hospital (n=155), (C) drug abusers (n=151), and (D) male homosexuals (n=187). ELISA positive sera were titrated and further examined by immunofluorescence and Western blot tests. ELISA tests using goat antihuman (IgA, IgG, IgM) serum were more sensitive than those using goat antihuman IgG serum.

HTLV-I antibody positive rates for these groups were: (A) 5.3%, (B) 9.0%, (C) 18.5%, and (D) 4.3%. HTLV-III antibody positive rates for these groups were: (A) 0.9%, (B) 4.5%, (C) 10.6%, and (D) 4.8%. The majority of individuals with positive tests were either reacting against HTLV-I or HTLV-III only. However, some individuals who belonged to groups C and D showed antibodies reacting against both viruses. These were confirmed by Western blot tests in which p19, p24, and env antigens of HTLV-I as well as p17, p24, p41, and gp160 antigens of HTLV-III were reactive with these sera. These preliminary results suggest the possible occurrence of concomitant infection in these individuals with both HTLV-I and HTLV-III, although other possibilities such as past sequential infections, and presence of cross reacting antibodies against viral or cellular antigens can not be excluded.

MP.96 Epidemiology of HIV Infection in Martinique, French Department in the West Indies.

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Since August 1985, 15207 blood donations from volonteer blood donors and 1399 high-risk people were tested using "ELAVIA" first generation assay. Positive specimen were retested by Indirect Immunofluorescence on fixed cells and confirmed with Western Blot (Pasteur) and Recombinant Env/Core protein assay (Abbott) All confirmed seropositive people were clinically evaluated and assessed for blood cell count, T Lymphocyte numbers and ratios, serum immunoglobulin and Beta 2-immunoglobulin levels, TPHA and Hepatitis B serologicals status and cutaneous multipuncture tests (Merieux).

Blood donors were compared to heathly controls. 0,2 % of blood donors and 6 % of patients were positive whose 15 with AIDS. In blood donors, among 83 reproductible Elavia test, 23 were Western Blot negative and 30 uninterpretable. Are they seroconversion or due to other retrovirus ? Recombinant proteins assay agree with Western Blot.

In 50 % of the donors, no usual risk factors have been founded, but heterosexual transmision could been involved. 70 % of the subjects had histories of S.T.D.

50 % of HIV positive, non-AIDS people are clinically asymptomatic, but have biological abnormalities. The average of T Helper cells is significantly higher for controls than for HIV positive.

The epidemiological caracteristics seems to be intermediary between those existing in France and the United States on one hand and Haïti and Africa on the other (heterosexual contamination and sex-ratio).

MP.97 Synthetic env- and gag- Peptides Are Recognized by HIV-specific Antibodies

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First generation of HIV-antibody diagnostic kits may be biohazardous and require verification due to strong immunochemical heterogeneity of the test systems. In order to solve these problems we synthesized peptide antigenic determinants specific for the products of "env" and "gag" HIV gene expression and produced monoclonal antibodies against some epitopes of HIV structural proteins. Env- and gag-specific structures were recognized among the produced spectrum of peptides with the help of commercial sera which gave the extinctions comparable with those obtained with the whole virus particles on polysterene.

Immunizing splenocyte cultures in vitro by whole immobilized virus or by the synthetic peptides we obtained HIV-specific monoclonals.

We are studying the possibility of producing ELISA systems on the basis of "peptide-monoclonal Ab" pairs to be used instead of the complicated systems of the first generation which require immunoblotting with whole virus proteins.

MP.98 Cutaneous and plasmatic Von Willebrand factor in AIDS : a marker of endothelial stimulation ?

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Patients infected by the human immune deficiency virus (HIV) (lymphadenopathy syndrome (LAS), Kaposi's sarcoma (KS), opportunistic infection (OI)) represent a model in which endothelial stimulation is important.

We studied plasmatic values of Von Willebrand factor (VWF) as an indicator of endothelial stimulation in 45 LAS, 23 AIDS KS and 9 AIDS OI in comparison with 19 normal controls and 12 classical KS. VWF was found to be elevated in AIDS OI ($P < 10^{-7}$) and AIDS KS ($P < 10^{-6}$) and at a lesser extent in classical KS ($P < 10^{-3}$) and LAS ($P < 10^{-2}$). No correlation was found between plasmatic VWF and a number of clinical and biological parameters : inflammation, immunological status, age, tumoral Burden, renal and hepatic functions. This elevation seems more to be linked to symptomatic or asymptomatic infections than to the KS itself.

To ascertain the diffuse vascular proliferation in these situations, we studied the number of vessels within the superficial dermis of clinically uninvolved skin by an indirect immunoperoxidase method using an antibody directed against VWF in 20 LAS & 10 AIDS KS in comparison to 11 controls and 10 classical KS. An increase in the number of vessels was found in LAS ($p < 0.01$), AIDS KS ($p < 0.01$) and classical KS ($p < 0.05$) suggesting that the endothelial stimulation is a diffuse mechanism in these situations.

The absence of correlation between plasmatic VWF and cutaneous vascular hyperplasia suggests that plasmatic VWF may be a good marker of endothelial dammage but a poor marker of vascular proliferation.

MP.99 Activated T-cells and neopterin in HIV-infection.

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Neopterin is a low molecular weight metabolite which derives from guanosintriphosphate. In vitro, it is produced from human monocytes specifically upon stimulation with interferon gamma. Extended studies confirm neopterin also in vivo to be a sensitive marker for the cellular immune activation status. It is characteristic for T-cell activation, interferon gamma production and monocyte activation. However, this does not implicate successful effector mechanisms.-Activation of T-cells is the central event regulating HIV-propagation and cell death in vitro. Our data, based mainly on neopterin measurements, allow the following conclusion in HIV-infection: 1) Activation of T-cells and monocytes parallels progressive HIV-infection. 2) Neopterin elevation reveals prognostic information. 3) There exists a significant inverse correlation of neopterin levels and CD4+/CD8+ ratio in AIDS patients. 4) In a significant percentage of seronegative members of high AIDS incidence groups neopterin elevation is preexisting. T-cell activation as predisposing factor for HIV-infection and progressive disease is also demonstratable in recipients of blood transfusion, in pregnant women and in children. Our data indicate: Activated T-cells are important for HIV-propagation also in vivo. Neopterin measurement is of potent tool in classifying and monitoring of patients infected with HIV.

MP.100 Abnormal B-Cell Differentiation Response to Polyclonal B-Cell Activators and Recombinant IL2 in AIDS and Pre-AIDS

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In AIDS, elevated serum Ig levels and autoimmune phenomena indicate B-cell activation in vivo. Reports of HIV-infected/ activated B cells give evidence for T-cell independent B-cell abnormalities. In order to characterize the B-cell dysfunction and conditions for its modulation, functional studies were done in 10 patients with frank AIDS and in 10 patients with persistent generalized lymph node enlargement (PGL) and HIV-positive sera. The control consisted of healthy heterosexual men. The in vitro experiments to assess the differentiation response were done with mononuclear cells and highly purified B cells. The Ig secretion into culture supernatants was measured by ELISA. In 7 day cultures the cells were stimulated with a T-cell independent polyclonal B-cell activator (Klebsiella pneumoniae, KlebsM) and with rIL2. All patients with AIDS failed to respond to these stimulants. rIL2 allone did not increase the Ig levels in patients with PGL and in the normal control. However, coculture experiments using KlebsM and rIL2 showed a pronounced increase of Ig levels in contrast to stimulation with KlebsM. This indicates an abnormal B-cell differentiation response in AIDS, which is T-cell independent and independent of exogeneous rIL2. However, in patients with Pre-AIDS,B-cell function can be modulated. These results implicate that treatment of HIV-infected individuals by rIL2 affects not only the NK-cell/T-cell system but also the B-cell system.

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MP.101 Abnormal Distribution of IgG Subclasses in AIDS and Pre-AIDS

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In AIDS, elevated serum Ig levels and autoimmunephenomena indicate B-cell activation in vivo. This might be a result of infection/ activation by HIV. In order to describe the characteristics of hypergammaglobulinaemia, especially of the predominant IgG isotype, we studied the distribution of the IgG subclasses in vivo and in vitro. The in vitro experiments consisted of 7 day lymphocyte cultures stimulated with T-cell dependent (PWM) and T-cell independent (Klebsiella pneumoniae, KlebsM) polyclonal B-cell activators (PBAs). The IgG subclasses were measured by ELISA. The cultures were done with 8 patients with frank AIDS, 8 patients with persistent generalized lymph node enlargement (PGL) and a normal control. In all patients sera, we found the hypergammaglobulinaemia restricted mainly to IgG1. Only in patients with PGL, elevated spontaneous Ig levels in vitro were increased under stimulatory conditions, as demonstrated by the measurement of all 4 subclasses in the culture supernatants. AIDS patients did not respond to the stimulants. According to the findings in sera of patients with PGL, the increase of total IgG after stimulation resulted mainly from IgG1. These data indicate a B-cell activation in AIDS and Pre-AIDS, that is restricted mainly to one IgG subclass, namely IgG1.

(Supported by the BGA/BMFT 'AIDS')

MP.102 Oral Bacteria Stimulation of Production of HIV.

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After blood, saliva was the second body fluid from which human immunodeficiency virus (HIV) was isolated. The origin of salivary HIV are infected lymphocytes from the gingiva. These cells emigrate into the saliva at a rate of 10^6 per minute. This emigration may increase up to 10-fold in oral diseases which are frequent in an immunocompromized host. Recent immunocytochemical studies show a higher incidence of HIV in salivary lymphocytes (SL) than in peripheral blood lymphocytes (PBL) of dental patients with AIDS. This suggests that the infected lymphocytes receive an antigenic and/or mitogenic stimulation by the oral flora resulting in a higher expression of the virus. To test this hypothesis we have studied the stimulation of HIV in CEM and AD1.3 permissive cell lines and PBL with cellular and cell-free fractions of autologous and allogenic saliva and several cultured bacterial species considered as periodontal pathogens. The stimulation was followed by immunofluorescence and immunoelectron microscopy techniques and by reverse transcriptase assay. Oral species known as inducers of lymphoblastic transformation show higher capacity for stimulation of the production of HIV. Opposite results were obtained with bacterial species suppressing lymphoblastic transformation. The use of saliva for detection of HIV infection offers the following advantages: a) collection of the specimens does not require a medical competence: b) quantity necessary for test can be easily collected: c) high concentration of the virus allows easy detection of the infection. It must be emphasized that successful attempts to isolate the virus by culturing, which is associated with separation of salivary fractions, must also include elimination of fraction which suppresses the lymphoblastic transformation.

MP.103 Cross Reactive Recognition of Different Human T Lymphotropic Retroviruses by HTLV-I and HTLV-III/ LAV Specific Cytotoxic T Lymphocytes (CTL).

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The precise characteristics of the cellular response to viruses of the human T lymphotropic retrovirus family, including HTLV-I and HTLV-III/LAV, have not yet been well defined. Recent studies have demonstrated the fine specificity of antibodies in the circulation of seropositive individuals which in the presence of effector cells, selectively mediate antibody-dependent cellular cytotoxicity in a non cross-reactive manner against either HTLV-I or HTLV-III/LAV infected cells. Moreover, HLA-restricted HTLV-III/LAV specific CTLs have been detected in the peripheral blood of some HTLV-III/LAV seropositive individuals, and HTLV-I specific CTLs can be generated in vitro using mononuclear cells from individuals with HTLV-I associated adult T cell leukemia in remission. In this study, HTLV-III/LAV specific peripheral blood CTL and a long term cultured HTLV-I specific CTL line were used to examine whether these immune cells could lyse in a cross reactive manner T cells infected either with HTLV-I or HTLV-III/LAV. Both the HTLV-I and HTLV-III/LAV specific CTLs demonstrated the capacity to lyse, in an HLA-restricted manner, T cells infected with either of the two retroviruses. However, the CTLs failed to lyse HLA-matched target cells infected with other viruses including cytomegalovirus or Epstein-Barr virus. Thus, in contrast to the non-cross reactive specificities of serum antibodies, retrovirus-specific CTLs appear to recognize retrovirus-associated common antigenic determinants on different T lymphotropic retrovirus infected cells.

MP.104 Infection of Brain Cells with HTLV-III/LAV in vitro

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To understand the pathogenesis of the neurological disorders in AIDS patients it is important to determine the susceptibility of brain-derived cells to HTLV-III/LAV. We examined cultured cells of glial origin as potential targets for HTLV-III/LAV infection. Normal and neoplastic cell lines positive for glial fibrillary acidic protein (GFAP) and, with one exception, negative for T4 antigen originating from fetal brain, astrocytoma or glioblastoma, were used in these studies. Infection with HTLV-III/LAV was performed by cocultivation of these cell lines with a HTLV-IIIB-producer cell line (KE37/I2-IIIB) as well as by exposure of these cell cultures to cell-free culture fluid harvested from this virus-producing cell line. Using an Immunoperoxidase method for the detection of HTLV-III/LAV antigens, virus-positive cells could be detected both in the normal as well as in the neoplastic brain-derived cells. The HTLV-III/LAV-infected cells exhibited a reduced growth rate and an altered growth pattern compared to their noninfected counterparts. These results indicate, that cells of glial origin can be infected with HTLV-III/LAV and that virus can exert a cytopathic effect on these cells.

MP.105 DYSREGULATED LYMPHOCYTE ACTIVATION IN AIDS.

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Lymphocytes of patients with the acquired Immunodeficiency Syndrome (AIDS) often display phenotypic markers of activation yet fail to transform in response to mitogens and antigens. We examined the relationship among ^3H thymidine incorporation, interleukin-2 (IL-2) production, IL-2 receptor (IL-2R) expression and cell cycle progression stimulated and unstimulated lymphocytes of patients with AIDS (P) and controls (C). Peripheral blood mononuclear cells (PBMC) of P incorporated less ^3H thymidine in response to phytohemaglutinin (PHA) and Tetanus toxoid (TT) than did PBMC of C. (PHA: P=5335±1192cpm, C=51075±10120cpm $p<0.01$; TT: p=925±155cpm, C=4970±1268cpm $p<0.01$). IL-2 production in response to TT as measured by proliferation of a murine cytotoxic T lymphocyte line also was diminished in P when compared to C (0±0 U/ml vs 7.5±3.9 U/ml, $p<0.02$). Freshly obtained lymphocytes of P more frequently expressed IL-2R (12.2±3.8% vs. 2.5±0.4% $p<0.01$)) as detected by anti-Tac reactivity yet failed to increase IL-2R after stimulation with PHA or TT (Δ IL-2R PHA P=8.9±4.8%, C=30.0±10.4%, $p<0.05$, ΔIL-2R TT P=0.1±0.3, C=3.1±0.4%, $p<0.01$). In two experiments, cell cycle analysis using acridine orange and flow cytometry revealed increased spontaneous progression through G_1 by P lymphocytes and no difference in PHA-induced G_1 progression when compared to C. Thus lymphocytes of patients with AIDS are apparently activated in vivo. Failure to proliferate in response to mitogens or antigens may be attributable in part to a block in transition past the G_1 phase of the cell cycle.

MP.106 Prognostic Significance of Antilymphocyte Antibodies (ALA) in the Progression of the Acquired Immune Deficiency Syndrome (AIDS).

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A large number of individuals are presently known to have been infected with the human immunodeficiency virus (HIV) but their risk of developing AIDS is yet uncertain. So far, the number of T-helper lymphocytes has been the only marker used to assess status of immune deficiency and prognosis. Previously,we have demonstrated the presence of antilymphocyte antibodies in the sera of AIDS patients. These antibodies react against lymphocytes expressing antigens recognized by monoclonal antibodies OKT_4 (CD4) and OKT_{11} (CD2). In a comparative study, we have found significant levels of ALA in 88% of 200 AIDS patients and in only 8% of 50 non-AIDS patients and 2% of 60 healthy males. To determine whether the presence of ALA indicates progression to AIDS, we investigated their levels in patients with AIDS-related complex (ARC) and in healthy homosexuals. Of 45 ARC patients,who were all seropositive for HIV, 29 (64%) had significant levels of ALA and of these 17 (59%) progressed to AIDS during the term of this study (18-30 months),while 16 (36%) had no elevated levels of ALA and none progressed to AIDS. Comparison of the mean levels of ALA in progressor versus non-progressor ARC patients shows a significant correlation ($p < 0.001$) between the increase of ALA and progression to AIDS. Of 87 healthy homosexual males, 38 (44%) were seropositive for HIV and of these 42% had elevated ALA while of 49 (66%) seronegative for HIV only 6% had increased levels of ALA.Subsequently,5 of 17 (30%) patients that were HIV+, ALA+ developed clinical disease (1 AIDS, 4 ARC),while no patients that were HIV+, ALA- presented with clinical symptoms.The present studies show a direct correlation between increased levels of ALA and the progression of disease in HIV-infected individuals.

MP.107 HIV RECOMBINANT ANTIGEN NEUTRALIZATION ASSAY: A SUPPLEMENTAL TEST TO ELISA AND WESTERN BLOT. N. Rolon, T. Hill, R. Kissinger, A. Sito, J. Geltosky and J. Britz. Ortho Diagnostic Systems Inc., Raritan, NJ 08869

Among blood donors, the reactivity rate for the detection of antibody to Human Immunodeficiency Virus (HIV) is 0.1 to 1.5%. The Western Blot (WB) test, currently used for confirmation of repeatably reactive ELISA results identifies antibodies to specific HIV proteins. An alternative method to the subjective and cumbersome WB utilizes recombinant gene products from the envelope, core, and polymerase regions to neutralize ELISA reactive sera in solution. A dilution of an ELISA reactive specimen is preincubated with a mixture of the recombinant antigens and retested in the viral lysate ELISA. A decrease in absorbance of 50% or greater relative to a non-neutralized control verifies a specimen as positive. To date, over 200 WB confirmed specimens with varied banding patterns have been effectively neutralized. Of 24 ELISA reactive, WB negative, false positive samples tested, none showed neutralization greater than 15%. Correlation between WB and neutralization methods has been 100% consistent with patient diagnosis.

MP.108 Neurological Involvement in AIDS: Roles of Cytomegalovirus and Human Immunodeficiency Virus

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In 28 patients with AIDS, neurological complications occurred in 13 (81%) of 16 patients with retinitis and in 1 (8%) of 12 patients without retinitis ($P<0.01$, chi square test). The onset of complications coincided with the onset of cytomegalovirus (CMV) viremia or of retinitis. CMV was found in the leukocytes of 15 (88%) of 17 patients and in the spinal fluid of 1 (17%) of 6 patients. CMV titer in the leukocytes ranged between 10^{-4} to 10^{-9} plaque-forming units with higher values in acutely ill patients. AIDS patients had CMV in mononuclear cells more often than non-AIDS patients. Genomic analysis revealed that paired CMV strains isolated simultaneously from mononuclear and polymorphonuclear leukocytes of two patients with AIDS differ in their restriction fragment profiles with EcoRI, BglII, and ClaI enzymes.

Intra-blood-brain-barrier IgG synthesis was increased in 5 of 6 patients, and the five had neurological complications. Elevated ratio of viral antibody titer in the spinal fluid to that in the blood was found with CMV (ratio 3.0 to 6.5) as well as with human immunodeficiency virus (HIV) (ratio 3.2 to 27.0). In patients treated with 9-(1,3 dihydroxy-2propoxymethyl)guanine, retinitis improved in 12 of 14, neurological symptoms in 2 of 4, and viremia in 4 of 8 patients. As reported elsewhere, in vitro CMV enhances cell lysis in a $T4^+$ lymphoblastic line persistently infected with HIV. CMV thus appears as a cofactor in AIDS with HIV. Anti-CMV treatment may be beneficial to patients with acute neurological involvement.

MP.109 Intra-blood-brain barrier (BBB) IgG synthesis (rate and CSF oligoclonal IgG bands (OB)) and abnormal serum bands (ASB) in patients with AIDS, ARC and asymptomatic HTLV-III-positive compared to normals.

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Intra-BBB IgG synthesis was determined for HTLV-III-seropositive patients with AIDS, ARC, or asymptomatic and for normals by an elevated rate formula and/or the presence of OB, (bands not present in or less intense in matched serum) by isoelectric focusing (IEF). 80% (12/15) of patients with AIDS Dementia Complex (ADC), 60% (3/5) of patients with known CNS opportunistic infections, and 60% (3/5) of neurologically asymptomatic patients had intra-BBB IgG synthesis. 62% (8/13) of patients with ADC, 60% (3/5) of patients with known CNS opportunistic infections, and 80% (4/5) of neurologically asymptomatic patients had ASB. Patients with ASB and/or CSF OB had an average number of 7 bands in each category. 80% (8/10) patients had an average of 63% of CSF OB corresponding to ASB but which were more intense in CSF. 7% (4/55) of normals had CSF OB (av. of 7 bands) and/or elevated rate and only 1 patient had 1 ASB. The data suggest that the majority of HTLV-III seropositive patients, at all stages of disease development and irrespective of neurologic disease, have an elevated intra-BBB IgG synthesis rate, OB, and a striking elevated number of ASB compared to seronegative individuals. Elevated synthesis may be indicative of a specific HTLV-III CNS infection and may possibly be a reflection of impending neurologic disease in neurologically asymptomatic patients. ASB are probably due to polyclonal B-cell activation in the systemic immune system. These bands are also be seen in the CSF, with less or equal intensity, due to diffusion of IgG from the blood. It is necessary to perform IEF on CSF and matched serum with serum diluted to the same IgG concentration as the CSF.

MP.110 Immunoglobulin Isotype Abnormalities in Pediatric Human Immunodeficiency Virus (HIV) Infection. JOSEPH A. CHURCH, Childrens Hospital of Los Angeles and USC School of Medicine, Los Angeles, CA, USA.

Hyperimmunoglobulinemia (Hyper Ig) is a common feature of HIV infection. However, Ig isotype deficiencies have also been noted in sporadic case reports. This study evaluated Ig isotype concentrations in 31 HIV-infected children, 22M, 9 F, ages 0.2 to 11 years (mean = 2.5 years) at diagnosis (Dx). AIDS was diagnosed in 17, AIDS-related disorders in 10, and four patients (pts) were asymptomatic. Risk factors included blood transfusions in 17 and parental high-risk in 14. IgG, IgA and IgM were measured in all pts with a nephelometric assay; IgG subclasses were measured in 19 pts with an immunoradiometric technique (Specialty Laboratories, Los Angeles, CA). Results were compared to age-adjusted normal values.

	↑IgG	↑IgA	↑IgM	↓IgG1	↓IgG1 + IgG3
AIDS	12/17	11/17	5/17	3/9	1/9
ARC	9/10	6/10	2/10	1/7	4/7
Asymptomatic	2/4	1/4	0/4	2/3	0/3

IgG deficiency was seen in one AIDS pt at Dx and three terminally. IgG subclass deficiencies were seen in five at Dx: IgG1 and IgG2 + IgG4 in two and one AIDS pts, respectively; and IgG2 and IgG4 in two asymptomatic pts, respectively. IgG1 + IgG2 deficiency and IgG2 + IgG4 deficiency were seen in two AIDS pts terminally.

In summary, the hyper Ig of HIV infection primarily involves total IgG and IgA levels; IgG1 and IgG3 are selectively increased in pts with hyper IgG; IgG subclass deficiencies were found in seven pts including two asymptomatic individuals.

MP.111 Primary infection with Human Immunodeficiency Virus: Clinical and Laboratory Features of 73 Cases.

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In an ongoing prospective study being conducted since November 1982, a total of approximately 600 homosexual men have been seen by their general practitioners and have undergone laboratory and HIV antibody testing every 6 months. Of all 345 men who were HIV negative at enrolment, a total of 73 (21%) have seroconverted by the time of this analysis. Dates of seroconversion were estimated for these individuals by taking the midpoint of the interval between the last negative and first positive anti-HIV test result. Paired comparisons of results obtained a mean of 5.3 months before and after seroconversion, revealed that an increase in mean IgG from 1138 to 1373 ($p < .001$), an increase in mean IgA from 181 to 190 ($p=.034$), an increase in mean C1q binding from 8.8% to 16.4% ($p<.001$) and an increase in mean CD8 count from 550 to 695 ($p=.067$), as well as a decrease in mean CD4/CD8 ratio from 1.67 to 1.34 ($p=.023$), and a decrease in mean WBC from 6468 to 5870 ($p=.005$), were associated with seroconversion. The mean CD4 count did not fall significantly with seroconversion (895 to 873; $p=.79$). Symptoms including fatigue, fever, night sweats, unintentional weight loss, diarrhea, arthralgias, cough unrelated to smoking, dyspnea, oral thrush, herpes zoster, and skin rash, did not increase significantly with seroconversion. In men who were free of generalized lymphadenopathy (GL) at enrolment, 14 (61%) of 23 seroconverters developed GL around the time of seroconversion as compared to only 11 (7%) of 151 persistently seronegative men during the same time period ($p<.0001$). These data suggest that elevation of the CD8 count and a resultant fall in the CD4/CD8 ratio as well as elevations of immune complex levels, IgG, and IgA, are early effects of HIV. It appears that CD4 cell depletion does not occur early and thus may be a longer term effect of this infection. The rarity of symptoms suggests that the majority of acute HIV infections may be asymptomatic or associated with only relatively minor symptoms, with the exception of generalized lymphadenopathy which appears to accompany a proportion of acute infections.

MP.112 Effect of Phorbol Myristate Acetate on T-cell colony growth from patients with AIDS, lymphadenopathy Syndrome (LAS) and seropositive homosexuals. M. ALLOUCHE*, Y. LUNARDI-ISKANDAR*, C. VARELA-MILLOT*, V. GEORGOULIAS*, W. ROZENBAUM**,CLAUDE JASMIN* et al., *INSERM U 268, Hop. P. Brousse, BP 200, 94804 Villejuif, FRANCE;** Sce Mal. Tropicales, Hop. Salpétrière, Paris, FRANCE.

We have shown previously that T-cell colony growth from peripheral blood mononuclear cells (PBMC) of patients with AIDS, LAS and from asymptomatic seropositive male homosexuals was impaired (1,2). In those experiments, T colony formation was induced with PHA-LCM, a medium conditioned by mitogen-stimulated normal PBMC. We thus investigated whether Phorbol Myristate Acetate (PMA)could synergize with PHA-LCM to enhance and/or restore T cell colony growth. In 8 out of 12 AIDS, and 4 out of 12 LAS patients, addition of PMA decreased the plating efficiency whereas in 12 normal heterosexuals, and in 5 out of 6 seropositive male homosexuals PMA maintained or increased the number and size of colonies. The phenotype of colonies induced by PMA+PHALCM was approximately the same in infected and non-infected subjects: T3 and T4 were expressed on less than 20% cells, T8 ranged from 22 to 55% and T11 was always expressed on more than 75% cells. The Tac antigen (IL2-receptor, IL2-R) was found on 38-97% cells in 2 AIDS and 4 LAS patients, as compared to 14-80% Tac^+ colony cells in normal heterosexuals. In contrast, incubation of PBMC with 10 ng/ml PMA in liquid culture failed to induce IL2-R expression in 4 out of 6 AIDS, 5 out of 11 LAS, and 2 out of 6 seropositive homosexual patients respectively, whereas in normal subjects 11-39% of PBMC became Tac positive. These results indicate that T cell colony growth and T-cell activation are deeply impaired in AIDS and LAS patients.

1) Clin. Exp. Immunol., 1985, 60, 285-293; 2) Blood, 1986, 67, 1063-1069.

MP.113 Ecto-5'nucleotidase Activities in Mononuclear Cells, T- and B-lymphocytes from Patients with ARC/AIDS and from Clinical Healthy Persons with HIV-antibodies.

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Decreased activity of the cell-membrane enzyme ecto-5'nucleotidase (ecto-5'NUC) has been found in mononuclear cells from patients with infections or different types of immunodeficiencies. The aim of this study was to describe the activity of ecto-5'NUC in patients with HIV antibodies and compare the level to the mito- and antigene induced proliferation of mononuclear cells.

In the present study the activity of the enzyme have been investigated in mononuclear cells, T- and B-lymphocytes from patients with ARC/AIDS and from clinical healthy homosexual men with antibodies against HIV. Mononuclear cells were prepared by density gradient centrifugation of frech venous blood and seperated in T- and B-lymphocytes by fluorescens activated cell sorting. Ecto-5'NUC vas measured by a radioactive method.

Mononuclear cells from AIDS/ARC patients showed reduced activity of ecto-5'NUC, the T-cell ecto-5'NUC was moderate reduced but all AIDS patients had B-cell ecto-5'NUC below the normal range lower limit. In the group of patients with antibodies against HIV but without clinical and amnestic signs of immunodeficiency the activity in the T-lymphocytes was within the normal range, but some of them sbowed decreased level in B-lymphocytes. Decreased B-cell ecto-5'NUC was correlated to reduced proliferation after in vitro stimulation or mononuclear cells with mito- and antigenes.

In conclusion: in patients with antibodies against HIV, decreased ecto-5'NUC activity in B-lymphocytes is correlated to the immunodeficiency, whereas AIDS patients with severe immunodeficiency ofteh had normal activity in T-cells.

MP.114 The Frequency and Characterization of Oligoclonal Protein (OCP) Bands in Individuals with HIV Antibodies

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Sera from 20 adults with HIV antibodies were selected for determination of the incidence and isotype of oligoclonal proteins (OCP), and the relationship of these bands to serum concentrations of IgG, IgA, IgM, C3 and C4. HIV antibodies were assayed with ELISA and Western Blot. OCP were characterized by immunofixation with H or L chain-specific antisera. Protein quantitation was performed with rate nephelometry.

OCPs were found in 13/20 (65%) of anti-HIV reactive sera. These OCPs were: G,K (3 samples); G,L (3 samples); G,K and G,L (6 samples); and K and L without an identifiable H chain (1 sample). No IgA or IgM OCPs were evident. The mean [IgG] for the OCP+ sera was significantly elevated (see Table) in comparison to both the reference range and the mean [IgG] for the OCP- sera. Mean serum levels of IgA and IgM were similar for both OCP+ and OCP- samples. There were, however, 9/20 individual sera with elevated IgA (332-929 mg/dl) and 5/20 sera with elevated IgM (387-595 mg/dl). Nevertheless, the increased levels of these isotypes were strictly polyclonal in character. The [C3] and [C4] for most samples were within the reference ranges. No striking differences in complement levels were associated with the presence of oligoclonal bands or with elevated immunoglobulins.

mg/dl:	G	A	M	C3	C4
Ref Range	540-1380	70-312	56-352	83-177	15-45
OCP(+)	2896± 495	289± 55	266± 45	110± 11	27± 5
OCP(-)	1632± 236	427± 91	217± 55	112± 8	31± 4
p:OCP + to -	0.0344	0.1856	0.5079	0.9179	0.6503

MP.115 ANTICARDIOLIPIN ANTIBODY, NEUROLOGIC COMPLICATIONS AND HIV INFECTION

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Serologic evidence of antibodies directed against cardiolipin (ACLA), one of many antiphospholipid antibodies, have been associated with thromboembolism, recurrent abortion and a variety of neurologic disease. Lupus inhibitors, also antiphospholipid antibodies, have been described in patients infected with HIV and opportunistic infection. We measured ACLA IgG by an enzyme-linked immunosorbant assay in 11 patients with HIV infection and either neurologic abnormalities, thromboembolism or recurrent abortion. Normal values were established in our laboratory. Raw data was transformed into a binding index (BI) by the method of Loizou (Clin exp Immunol (1985) 62,738-745). A positive value is defined as BI > 3 standard deviations above the mean (0.86 +/- 3(.58) = 2.6). Only 2 patients had immune deficiency and none had opportunistic infection. All but 1 patient had abnormal ACLA IgG values. The clinical syndromes represented are as follows: thrombosis in 1, recurrent abortions in 1, headaches in 3, neuropsychiatric symptoms in 4, herpes zoster in 1, peripheral neuropathy in 1. ACLA IgG value in this last patient was normal prior to the development of his neuropathy, but became abnormal 4 months after his symptoms began. These observations demonstrate that antiphospholipid antibodies are not limited only to patients infected with HIV and opportunistic organisms. A relationship between these antibodies and neurologic symptoms in HIV infection is suggested.

MP.116 The Biopsychosocial Research Center on AIDS: A Multidisciplinary Approach to the Investigation of the AIDS Disease.

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Seven major studies are currently being conducted at the center. The objective of this research is to conduct a multidisciplinary, longitudinal study of the AIDS disease which examines several HIV positive groups from a psychoneuroimmunological perspective. The center is organized so that common strategies, procedures and data are utilized by all studies. Similarly, a thematic emphasis is shared by all center components; factors are examined that influence the transmission of disease, mediate the likelihood of increased pathology, and influence the course of infection.

The studies focus on: the psychosocial co-factors and cognitive AIDS-related dementia in an HIV positive, homosexual population; the neurological aspects of pediatric HIV infection; predisposing factors, course and rate of deterioration following HIV exposure in a population of I.V. drug abusers; the effect of an exercise intervention in a population of HIV- positive and negative gay men; an intervention study which examines the prevalence and specific risk factors associated with the presence of antibodies to the virus in both HIV positive and negative I.V. drug abusers; the role of nutritional factors in the development of AIDS in an HIV positive population; and, attitudes toward AIDS and health care practices among a Haitian population. Variable assessment is extensive and wide-ranging. Preliminary data will be presented from each study.

MP.117 EBV and HIV Antibodies in Broncho-Alveolar Lavage (BAL) and in Serum of HIV Positive Children with or without Pulmonary Lymphoid Hyperplasia/Lymphoid Interstitial Pneumonitis(PHL/LIP)Complex. A Causal Association ?

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The PLH/LIP complex is a common finding in children with AIDS. The role of EBV activation in determination of LIP has been recently suggested.

To assess the profile of EBV and HIV antibodies in HIV-positive children presenting with pulmonary pathology, we investigated BAL in 27 consecutive patients. Out of those,for the last 13, we titered antibodies to HIV and EBV by immunofluorescence, both in serum and BAL. From the clinical view point, 5 had PLH/LIP complex, 3 Pneumocystis carinii (PC), 2 other opportunistic infections (OI) and 3 had ARC. 4/5 of LIP cases had serum EBV profile suggesting viral activation (IgG EA : high titers, IgA VCA : traces). 1/5 had normal EBV immunity. In BAL, IgG VCA were detected in 3/5 LIP. In the 5 LIP cases, HIV antibody titers were significantly higher than in non-LIP patients ($p < 0,001$). In the 8 non-LIP children, 6 (3 ARC , 2 OI, 1 PC) had no EBV antibodies at all, 1 had a profile of recent infection, 1 normal immunity. The CD4/CD8 ratio in BAL (monoclonal antibodies staining, immunoperoxydase technic) was very low in all HIV positive children , regardless to pulmonary pathology : 0,20 ± 0,11 as compared to 0,87 ± 0,15 in normal children ($p < 0,001$) but the absolute number of CD8 cells recovered by BAL was very significantly higher in LIP patients. In pulmonary biopsies of LIP cases, we observed large predominance of CD8 lymphocytes with very few B lymphocytes.

EBV activation may represent a critical cofactor enhancing both CD8 lymphoid pulmonary infiltration and HIV replication in children with PLH/LIP complex.

MP.118 Leu7 (HNK-1) Cells In AIDS And Related Syndromes.

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Leu7 (HNK-1) is a monoclonal antibody initially described as specific of human natural killer cells. Previous reports have related elevations of the lymphocyte subset defined by this marker to viral infections. We investigated this specific subset, in comparison with classical T-cell markers (CD3, CD4, CD8), in a population of 151 HIV-seropositive patients. AIDS was diagnosed upon clinical examination in 26 of these patients. A total number of 235 analyses was performed, using classical indirect immunofluorescence techniques on peripheral lymphocytes isolated by Ficoll gradient centrifugation. Percentages and absolute numbers of each subset were plotted and compared. Classical profiles were obtained for CD3 and CD4, significantly lower in AIDS patients. The mean percentage and absolute number of Leu7+ cells was increased in non-AIDS seropositive patients, compared to normal controls (respectively 20.3% - 303 cells/mm^3 and 10% - 255 cells/mm^3). In AIDS patients, the percentage of Leu7+ cells remained elevated, while their number was significantly lowered. No significant correlation was observed between this subset and the CD8+ subset. In conclusion, our data indicate the participation of a lymphocyte subset involved in anti-viral mechanisms in the early stages of HIV infection.

MP.119 Characterization of the latent period and the development of neutralizing antibodies in early sexually transmitted HIV infection.

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We have prospectively followed immunological and virological events in 15 Finnish men who contracted HIV infection through sex and seroconverted. A common finding was a latent period, lasting for 4 to 18 months, when only viral antigen (sandwich EIA) or anti-gag antibodies alone (Western blot and CIA-RA) were seen.Clinically, no symptoms except for an abrupt seborrheic dermatitis in some were recorded. During this time, T_H cell numbers were normal but a defect was seen in cell mediated immunity to soluble recall antigens in half of the cases, and in no one neutralizing antibodies could be detected with the sensitive ATH-8 cell microassay. Using RNA in situ hybridization, rare positive cells of monocyte-dendritic cell lineage were seen. In the majority of the cases a full blown anti-viral antibody response developed first after a verified DNA virus (EBV, HBV, CMV) infection whereafter T_H cells started to diminish. It is possible that these viruses enhance HIV replication by transactivation. Neutralizing antibodies appeared first after the full seroconversion, and the highest neutralizing titers were reached along with the development of lymphadenopathy. A fourfold rise in the neutralizing antibody titer during the follow-up period favoured a nonprogressive clinical course.

MP.120 Human-Immunodeficency Virus Induced Hyperimmunoglobulinemia and Its Associations with CD5 (Leu 1) Expression on B Cells.

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We hypothesized that elevated immunoglobulins in HIV-infected subjects were related to the increased proportions of CD5+ (Leu 1+) B cells, human equivalents to the Lyt1+ B cells in mouse disease models. Analysis of circulating levels of IgG, and IgA in healthy controls and HIV infected individuals indicated that there was a significant ($p<0.01$) correlation ($r=0.67$ and 0.42, respectively) with the proportions of CD5+ B cells in peripheral blood. Individuals infected with HIV had significantly ($p<0.001$) greater proportions of B cells expressing CD5 and total serum immunoglobulins than did healthy controls. These changes were directly related to the severity of the disease state of the HIV seropositive individuals (healthy homosexuals <AIDS related complex <AIDS). The proportions of B cells expressing CD5 were significantly ($p<0.001$) and negatively correlated ($r=-0.52$) to the T helper/suppressor-cytotoxic ratio. We observed a significant ($p<0.0001$) negative correlation ($r=-0.82$) between the proportions of both the suppressor-inducer T cells (CD4+/2H4+) and the B-cell differentiation factor secreting T cells (CD4+/HB11-). Neither the elevated immunoglobulins nor the increased proportions of CD5+ bearing B cells were significantly correlated to the proportions of helper-inducer (CD4+/4B4+) or suppressor-inducer (CD4+/2H4+) T cells. We conclude from these data that hyperimmunoglobulinemia is strongly associated with the increased proportions of CD5 expressing B cells and that these elevations are probably caused by direct-HIV effects on B cells rather than indirectly by the altered balance of immunoregulatory T-cell subsets.

MP.121 The Sequential Loss of T Cell Functions Following HIV Infections.

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During the course of HIV infection, there appears to be a sequential loss of T cell functions. To test this, the present studies examined four groups of homosexual men: HIV antibody-negative (Ab-) (150); recent Ab seroconverters (15); HIV Ab+ asymptomatic men (50) and those Ab+ men with chronic adenopathy (68). The recent seroconverters were studied 2-19 months after their last negative Ab test (mean 9 months). Data are presented below.

	%IL-2R Cells	T cell Colonies	No with T4 <400/mm^3	IL-2 Synthesis (U/ml)
Ab-	41.1	4421	8.8%	18.6
Ab converters	28.2*	4301	14.3	----
Ab+	25.0*	2608*	19.0	31.7
Adenopathy	25.2*	2412*	26.2*	16.2

*Significantly different from Ab- group

Thus, an early effect of infection is reduced ability of PHA stimulated cells to express IL-2 receptors; this is seen in recent seroconverters. Shortly thereafter, T colony growth is depressed; this can be seen in asymptomatic homosexuals with normal numbers of T4 cells. T4 lymphopenia and decreased IL-2 production are later events. Colony responses correlate with the number of T4 cells and the expression of IL-2 receptors. These results suggest defective ability to express IL-2 receptors and reduced T colony formation reflect immune abnormalities associated with recent HIV infection.

MP.122 Cell-Mediated Cytotoxicity Against Human Immunodeficiency Virus-Producing Cells

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The cell-mediated immune response to human immunodeficiency virus (HIV) infection has not yet been studied sufficiently to clarify differences between the host defence mechanisms of healthy persons and of HIV-seropositive individuals. Here we report that peripheral blood mononuclear leucocytes (PBL) from healthy persons and also to some extent from HIV-seropositive patients (with or without an HIV-associated disease) possess in vitro cellular cytotoxicity to HIV-producing cells in the presence of antibodies against HIV-related antigens. This antibody-dependent cell-mediated cytotoxicity of PBL is proportional to the concentration of specific antibody, but the specific antibody alone is not lytic for HIV-producing cells. Interestingly, lymphokine-activated killer (LAK) cells also appear to display a potent cytotoxic action against HIV-producing cells. Boosting these cell-mediated defence mechanisms could be a useful therapeutic intervention in patients with the acquired immunodeficiency syndrome.

MP.123 **T8-D44 POSITIVE LYMPHOCYTIC ALVEOLITIS IN HIV INFECTED PATIENTS**

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A T lymphocyte alveolitis has been demonstrated in patients with the Acquired Immunodeficiency Syndrom and Related Complex. We have further analysed the Broncho-Alveolar Lavage (8AL) fluid cells of patients seropositive for HIV. 9 patients with (2) or without (7) lung abnormalities were selected on 2 criteria : 1) a L.A. demonstrated in a 1st BAL fluid (mean lymphocytes : 55 %), 2) the absence of any lung infection or tumour. A 2nd BAL confirmed the L.A. in all patients. The alveolar lymphocytes and the peripheral blood lymphocytes (PBL) were then simultaneously double-stained with the D44 monoclonal antibodies (moAb) specific for cytotoxic T8 lymphocytes (1), the anti-T8, T4, T3 moAbs. The L.A. was composed of 74 % T8+ - D44+ lymphocytes. Both the T4/T8 and the T8+ D44+/T8 ratios were significantly decreased compared with the PBL values (p 0.005). Alveolar T8 cells were partially activated since only 8 % expressed the IL2 receptor. An immunoenzymatic analysis of the alveolar macrophages (A.M.) could be performed in 4 of these patients using the Leu 4 moAb and the CVK-A1 moAb specific for the p18-HIV antigen (2). Most of the A.M. were positive for both the T4 molecule and the p18-HIV antigen. These data suggest that in HIV infected patients, a L.A. could result from a pulmonary recruitment of phenotypically cytotoxic T8 lymphocytes and is associated with p18-bearing alveolar macrophages.

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MP.124 Persistent Human Immunodeficiency Virus (HIV) Detection in Seronegative Asymptomatic Carriers.

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We describe 4 asymptomatic HIV infected patients in whom no anti-HIV antibodies could be detected by any usual serological assays over a follow up period of 16 to 23 months. All patients were at risk of HIV infection. Evidence of HIV infection was demonstrated by culture of HIV from patients' lymphocytes associated with reverse transcriptase assay. For each patient, cultures were performed at least three times during the follow up period and were consistently positive. Serological assays for HIV antibodies consisted in enzyme-linked-immunosorbent assay, Western-Blot analysis, indirect immunofluorescence, radioimmuno precipitation assay. For each patient, detection of HIV antibodies was attempted on at least five occasions and remained negative. During the follow up period, lymphocytes counts, mitogens responses and T4/T8 ratios remained normal, except in one patient. This patient seroconverted after 23 months. This observation suggests that a HIV-carrier state without any detectable HIV-antibodies and without clinical and biological significant evolution can persist over extended periods of time, illustrating another aspect of the natural history of HIV infection.

MP.125 Subclass and Isotope Specific Antibody Responses to HIV Infection Analyzed by Western Blotting: Correlation with Clinical Status.

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To determine the fine specificity of antibody (Ab) responses to human immunodeficiency virus (HIV) infection, we constructed an HIV Western Blot (WB) using monoclonal Abs to each of the four immunoglobulin G (IgG) subclasses and to IgG, M, and A isotypes. We analyzed 37 healthy HIV seropositives (HHS) and 41 AIDS patients. Total IgG WB patterns did not differ between HHS and AIDS patients. However, a significantly greater proportion of HHS individuals had both IgG 1 and IgG 2 Ab to pol (p66, p53, p31) and gag (p55, p24, p15/17) antigens (Ags) when compared to AIDS patients. No significant differences between the two groups were seen with IgG 1 or IgG 2 Abs to env (gp160/120, gp41) Ags. IgG 3 responses were almost entirely restricted to gag Ags. However, there were no significant differences between the two groups of patients in the frequency of IgG 3 anti-gag responses. IgG 4 responses were relatively infrequent in both groups but were not restricted to any category of HIV Ags, nor did the frequency of IgG 4 antibodies to any HIV Ags differ between the two groups. IgM Ab responses in both groups were predominantly against p24 and were significantly more frequent in HHS (47%) than AIDS patients (22%) and IgM Abs to p64, p53, and p15/17 antigens were also significantly more frequent in HHS. Serum IgA Abs against most Ags were observed in <10% of patients, but 25% of HHS had IgA Ab to p24 versus 5% of AIDS patients. The detection of p24 antigen in serum or plasma by enzyme immunoassay correlated with a decreased frequency of both IgG 1 and IgM Abs to p24, but not to other HIV Ags. These differences in WB banding patterns correlate with clinical status and may be useful in predicting outcomes of HIV infection, and in delineating functional properties of anti-HIV Abs.

MP.126 Two T-cell Growth Factors Distinct from IL-2 Which Provide a Proliferative Advantage to CD4+ T-Lymphocytes.

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Two factors from a human T-cell lymphoma cell line, designated Leukemic T-cell Growth Factors I and II (L-TCGF I and II) will, like IL-2, support the growth of activated, but not resting, T-lymphocytes. These factors can be distinguished from human IL-2 and each other on the basis of molecular weight, isoelectric point, temperature stability, resistance to inactivation by proteolytic enzymes, and sensitivity to chemical reducing and chaotropic agents. Anti-IL-2 antibodies do not react with either L-TCGF, and concentrations of anti-IL-2 receptor antibody which inhibit greater than 95% of IL-2 activity do not inhibit the L-TCGFs.

IL-2 and the L-TCGFs appear to exert differential effects on T-cell subsets. Unlike IL-2, the L-TCGFs will not support the proliferation of a cloned mouse cytotoxic T-cell line, CTLL-2. In addition, whereas IL-2-supported long term growth of PHA-stimulated human T-lymphocytes yields populations enriched in CD8+ cells, culture of similar cells in the presence of L-TCGF I or II results in a predominance of CD4+ cells. These factors represent new interleukins structurally and functionally distinct from IL-2 which do not act through the IL-2 receptor. Their biological significance and possible role in HIV-associated immunodeficiency remain to be clarified.

MP.127 Antibody Response to Human Immunodeficiency Virus in Homosexual Men. Relation of Antibody Specificity, Titer, and Isotype to Clinical Status, Severity of Immunodeficiency, and Disease Progression.

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We tested serum samples from 107 homosexual or bisexual men who are seropositive for antibody to the human immunodeficiency virus (HIV) by Western blot for antibody titer to specific virus proteins. The isotype distribution of HIV antibody was also determined using monoclonal antibodies specific for IgM, IgA, and the IgG subclasses. Antibody titers to most viral proteins were lower in sera from patients with the acquired immunodeficiency syndrome (AIDS) and in sera from men whose condition subsequently progressed to AIDS than in sera from asymptomatic men and men with lymphadenopathy who have not progressed to AIDS. The exception was antibody titer to the transmembrane protein gp41, which was similar in all groups. We found no evidence of isotypic prominence or restriction of the antibody response. In multivariate analysis, lower levels of $T4^+$ T-helper cells were most highly associated with (or predictive of) progression to AIDS. Antibody titers correlated with $T4^+$ T-cell levels, and therefore, declining titers are in part a function (or consequence) of the severity of immunodeficiency. However, lower antibody titers to the envelope protein gp110, the core protein p24, and the reverse transcriptase enzyme p51/65 were also predictive of progression to AIDS independent of their association with $T4^+$ T-cell levels. These data suggest that differences in antibody levels are not simply a consequence of severe immunodeficiency but may have a role in (or are a marker for) control of infection.

MP.128 Kinetics of Interleukin-2 Augmentation of Natural Killer Cell Cytotoxicity in the Acquired Immunodeficiency Syndrome.

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Natural killer cytotoxicity (NKC) of peripheral blood mononuclear (PBM) cells is depressed among individuals with the acquired immunodeficiency syndrome (AIDS). In vitro incubation of PBM with Interleukin-2 (IL-2) leads to NKC augmentation, but not to the level of healthy controls. Therefore, the kinetics of IL-2 augmentation of NK in AIDS were evaluated. PBM from healthy adults and those with AIDS were incubated with interferons (1000U/ml) alpha ($rIFN\alpha_2$), beta ($rIFN\beta_{ser}$), rIL-2 (50U/ml), or with medium for 1-12 hrs prior to a 4-hour ^{51}Cr-release assay against K562 tumor targets. Mean lytic units ($LU/10^7$) of NKC were as follows.

	Controls (n = 14)		AIDS (n = 16)	
	1hr	12 hr	1 hr	12 hr
PBM	93	106	<5	<5[a]
rIFNβ	158[b]	413[a]	<5	<5
$rIFN\alpha_2$	178[b]	347[a]	<5	<5
rIL-2	231[b]	454[a]	8	55[c]

a = p <.05; b = p <.01 both from control PBM; c = p <.05 from AIDS PBM

Among both controls and AIDS PBM, the spontaneous NKC did not increase with incubation time. Significant augmentation of NKC among controls was observed with IFNs and IL-2 after 1- and 12 hours ($p<.05$; $p<.01$), while NKC was augmentated among PBM from AIDS only after ≥ 12-hours of incubation with IL-2. These data suggest that the kinetics of augmentation of NKC in AIDS are different from controls. Based upon these in vitro data, therapeutic regimens using IL-2 in AIDS may require more prolonged exposure to augment immune responses.

MP.129 Studies of "p24 Only" Immunoblot Reactivity to Human Immunodeficiency Virus.

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As a reference laboratory providing comprehensive ELISA and immunoblot testing of sera for the detection of antibody to Human Immunodeficiency Virus (HIV), we have become increasingly interested in the interpretation of immunoblot results that demonstrate reactivity with p24 but not gp 41 viral protein. In the present study, sera from 12 patients having p24 but not gp 41 or p55 reactivity to HIV antigen from Electro Nucleonics, Inc. (ENI) were retested using HIV antigen from Dupont containing high (>100,000 Daltons) as well as lower molecular weight viral proteins, ELISA (ENI) and indirect fluorescent antibody (IFA) techniques. Five of 12 sera showed p24 and gp 110/120 Dupont immunoblot reactivity and IFA reactivity. All but one of the 5 sera were also ELISA reactive. Subsequent sera were obtained from 2 of the 5 patients, including the patient with the ELISA negative serum, at 14 and 34 days after the initial specimens. These later specimens both demonstrated p24, gp 41, p55 and gp 110/120 reactivity on Dupont immunoblot as well as IFA and ELISA reactivity. Sera from the remaining 7 patients studied demonstrated p24 but not gp 110/120 Dupont immunoblot reactivity and were non-reactive by IFA. Only 1 of the 7 sera was reactive by ELISA which was determined to be non-specific. Subsequent sera obtained from 2 of the 7 patients after 25 and 28 days again demonstrated only p24 reactivity on Dupont immunoblot and were non-reactive by IFA and ELISA. Sera from all 12 patients were absorbed with H9 cell lysate and were tested by immunoblot for reactivity to HTLV-I and HTLV-II viral antigens. Absorbed sera retained HIV p24 reactivity. None of the sera demonstrated p24 reactivity with HTLV-I or HTLV-II antigen.

MP.130 HTLV-I Associated B Cell Transformation: A Model for the Study of AIDS-Related B Cell Lymphoma.

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The recent observation that sera from a high proportion of AIDS-related B cell lymphoma patients react with both HTLV-I and HIV proteins (Feigal, et al, this meeting) has led us to investigate one of five immortalized human B cell lines derived by cocultivation of a lethally irradiated HTLV-I infected and immortalized T cell line (CS-1) with normal human tonsillar cells. We found that this B cell line, HKA-3 expresses and secretes IgM, and produces HTLV-I envelope glycoprotein, gp61. Two dimensional gel electrophoresis further showed that secreted HKA-3 IgM had anti-GP61 activity. A mouse monoclonal anti-idiotypic antibody developed against HKA-3 IgM bound to cell surface forms of HKA-3 IgM and competed with HTLV-1 for cell binding. In vitro proliferation studies revealed that both purified HTLV-I and anti-idiotypic antibodies specifically increased HKA-3 cell proliferation, while control monoclonals and purified HIV had no effect. These studies describe an immortalized B cell line, HKA-3, transformed in association with HTLV-I, which produces its own antigen, gp61. Similar to normal B-lymphocytes, HKA-3 cells proliferate, at least in part in response to this antigen. Because HTLV-I may play a role in B cell transformation in vivo, this system may provide an interesting new in vitro model for the further investigation of AIDS-related B cell lymphomas.

MP.131 Isolation of HTLV-III/LAV Using Monocyte/Macrophages as Targets for the Virus.

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HTLV-III/LAV isolates have been recovered from brain and lung tissues of patients with AIDS. These tissues contained virus-positive cells which exhibited characteristics of mononuclear phagocytes. These isolates had a significantly higher ability to infect monocyte-macrophages (MM) than T cells. (Gartner, et.al., Science, 233:215, 1986 and JAMA, 256:2365, 1986) It is conceivable that this preferential tropism can account for the considerable variability in the isolation of the virus from specimens of HTLV-III/LAV-infected individuals utilizing conventional T cell culture techniques. Using peripheral blood-derived MM and T cells as targets for the virus, we attempted virus isolation from a number of specimens. Several isolates were recovered from brain, peripheral blood adherent cells, lung and skin using MM cells as targets. In most cases, we failed to isolate virus from these specimens using T cells for cocultivation. Isolates from peripheral blood T cells could be readily recovered by both MM and T cell targets. In contrast, isolates from thymic tissue were recovered by T cell but not by MM cell cocultivation. These results further suggest that different variants of HTLV-III/LAV exhibit a perferential tropism for MM or T cells. Furthermore, because the longevity and magnitude of virus production in MM cells exceeds that of T cells, MM cells are more efficient targets for virus rescue.

MP.132 Correction of Lymphocyte Dysfunctions in vitro in ARC and AIDS Patients as a Consequence of Isoprinosine Induced Changes in T_h Cell Subsets and Antigen Presenting Monocytes ($LeuM_3^+$ Ia^+).

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Peripheral blood leukocytes from ARC and AIDS patients were analyzed following PHA and PWM induced lymphocyte transformation with mAb(s) that identify developemental (HLA-DR) and functional T-cells and monocytes. Significant decreases in both suppressor regulating T_h subset ($Leu3^+$ $Leu8^+$) and the reciprocal inducer T_h subset ($Leu3^+$ $Leu8^-$) responsible for inducing differentiation of B cells were observed. Simultaneously, the percentage of effector T_s and the precursor T_s cells were increased, both of which were required for generation of suppression of cell mediated immunity. There was a selection of Ia^+ cells bearing Leu2 (Ts) markers and a concurrent reduction of antigen presenting monocytes and activated T_h cells. Data suggest that the functional deficiencies in AIDS may be caused by defects in T cell activation as well as antigen presentation by monocytes.

Isoprinosine stimulated B cell functions of ARC and AIDS patients, in a selective fashion restoring both T cell dependent PWM induced transformation and the spontaneous secretion of immunoglobulins by plasma cells while having no effects on resting B-cells. Isoprinosine induced an increase in regulator T_h ($Leu3^+$ $Leu8^+$) and inducer T_h ($Leu3^+$ $Leu8^-$) cells while potentiating Ia antigen on T_h and monocytes during blastogenesis. These events initiated a cascade of cellular interactions leading to restoration of cell-mediated immune responses. These interferences with the defective helper/suppressor regulatory pathways may have important therapeutic implications.

MP.133 Monocyte Function in a Male AIDS Patient and His Identical Twin Brother.

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To explore whether monocyte dysfunction may contribute to the impaired lymphocyte proliferative responses in AIDS, we compared the accessory cell function of monocytes from an AIDS patient with that of his healthy, heterosexual, identical twin brother. Monocytes and T lymphocytes from the twins were purified by counterflow centrifugal elutriation. The phytohemagglutinin (PHA)-induced proliferative response of the patient's lymphocytes in the presence of his own monocytes was 13,000 cpm whereas that of his brother's mononuclear cells was 102,500 cpm. However, replacement of the patient's monocytes with those of his healthy brother resulted in a 3-fold increase in PHA-stimulated lymphocyte DNA synthesis. In addition, the patient's monocytes produced <30% the interleukin 1 (IL-1) activity of his twin brother's monocytes. Therefore, we added purified exogenous IL-1 to cultures of the AIDS patient's T cells plus his defective monocytes which resulted in a 3-fold augmentation of DNA synthesis. Since the surface glycoprotein HLA-DR, a class II histocompatibility antigen, is required for accessory function, we also analyzed by fluorescence activated cell sorter the expression of HLA-DR on the monocytes from the twin subjects. Altbough the percentage of $HLA\text{-}DR^+$ monocytes was reduced in the AIDS patient (55%) compared with that of his brother (83%), the density of HLA-DR on the patient's monocytes was 2.5 times grester than that expressed on the brother's monocytes.

Thus, monocyte accessory cell function in an AIDS patient was reduced compared with that of his identical twin brother, and this reduction was due in part to reduced IL-1 secretion and not to reduced expression of HLA-DR. Accessory cell dysfunction may contribute to the immunosuppression in AIDS.

MP.134 Anti-class II antibodies in AIDS patients and AIDS risk groups.

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The specificity of anti-lymphocyte antibodies against class I and class II antigens was evaluated in AIDS patients and in individuals at risk of AIDS (R-AIDS: male homosexuals (Ho) and hemophiliacs (He)) with positive or negative serology for HIV.

Anti-class II antibodies capable of inducing antibody-dependent-cell-mediated cytotoxicity (ADCC) against non-T cells and B lymphoblastoid cell lines (P3HR-1K, Raji) were detected in AIDS patients and in R-AIDS with or without HIV infection. This finding was confirmed by experiments in which class II antigens in target cells were blocked with monoclonal anti-class II antibody (DA6.231) and the cytotoxic reaction induced by patient's sera was abolished.

In contrast, ADCC was not impaired by preincubating the target cells with monoclonal anti-class I antibody (W6/32). Prevalence of antibodies to non-T cells was confirmed by standard C-mediated microlymphocytotoxicity.

In addition to ADCC and C-mediated cytotoxicity, anti-class II and anti-class I antibodies were assayed by their ability to interfere the binding of fluorescein labelled anti-class II (HLA-DR, Becton Dickinson) and anti-class I (W6/32) antibodies to peripheral blood mononuclear leukocytes (PBMC), non-T cells, P3HR-1K and Raji. Anti-class II specificity was confirmed, and antibody titers tended to be higher in Ho than in He, using non-T cells and Raji as targets.

High titers of anti-class II antibodies could contribute to impair antigen recognition and aggravate the immune deficiency in this group of patients.

MP.135 Immunosuppressive Activity Associated with a Cell Line infected with HTLV-III.

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Supernatants from an HTLV-III-infected H9 cell line were found to contain a potent antiproliferative activity not found in supernatants of an uninfected H-9 counterpart. The activity inhibited the proliferation of PBL activated in vitro, as well as the growth of several cell lines, but was not directly cytotoxic. The activity was apparently not associated with intact HTLV virion in that it was found only in the supernatant and not the pellet fraction of a 100,000 x g; 2.0 hr. ultracentrifuged preparation of culture supernatant. Uninfected CEM cells would, upon being exposed to purified virus or pelleted virus from infected cell line supernatant, produce antiproliferative activity within one week postinfection. The activity was found to be protease sensitive; labile to heat (65°C; 30 min), unrelated to alpha or gamma interferon, and insensitive to indomethacin. Preliminary treatments of culture supernatant with several different antisera to HTLV-III proteins have failed to neutralize or immunoprecipitate the activity. Chromatography of concentrated supernatants elucidated major peaks of activity with apparent molecular weights of >200 kd, ~65 kd and 9-17 kd. A substantial degree of purification was obtained after affinity chromatography on hydoxyapatite, and active fractions eluted from this medium were used to immunize rabbits and mice, which produced antisera (IgG-fractions) capable of immunoprecipitating the antiproliferative activity.

MP.136 Malignant Prurigo of AIDS

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During the period July 1983, to December 1984, we observed that 66/134 (49%) Haitian AIDS patients had intensely pruritic skin lesions (prurigo) for which neither specific etiologic nor categorical diagnoses could be established. Comparable lesions were not noted in 127 siblings and friends, but were present in 6 HIV seropositive spouses of the AIDS patients. Prurigo was an initial manifestation in 79% of these 66 patients and appeared a mean of 8 months prior to the diagnosis of AIDS. Prurigo was characterized by multiple erythematous round macules or papules which first appeared on the extensor surface of the arms but subsequently involved the legs, trunk and face. Histologically the lesions were characterized by varying degrees of mixed (predominantly eosinophilic) perivascular inflammatory cell infiltrates of the dermis. The lesions did not respond to any therapeutic regimens employed and usually persisted throughout the AIDS illness. Demographic and laboratory data did not distinguish AIDS patients with prurigo from those without prurigo.

MP.137 CLINICAL AND IMMUNOLOGICAL FEATURES OF HETEROSEXUALS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV).

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An epidemic of HIV began in Edinburgh amongst heterosexual intravenous drug misusers (IDM), one third of whom are female, in August 1983 and reached 50% seropositivity by 1985. Edinburgh has a large cohort of HIV infected heterosexuals Only 40% of individuals infected via drug misuse are currently misusing.

We examined 115 HIV seropositive individuals, 5 homosexuals, 1 blood transfusion recipient, 3 heterosexual contacts of IDM and 106 IDM. Eighty two per cent of them have lymphadenopathy at two or more non-inguinal sites, 76/101 have elevated IgG levels, 4 have had clinically significant thrombocytopaenia, 15 have a leucopaenia <4.0x10(9)/l and 39 have a lymphopaenia <1.4x10(9)/l.

We performed lymphocyte subset estimation on 78 individuals and 22% have T4 cells <0.25x10(9)/l, 54% <0.5x10(9)/l and 83% <0.9x10(9)/l. There was no excess of current misusers or females in any of the catergories. Significantly a total white cell count missed 71% of patients with a lymphopaenia and a total lymphocyte count missed 41% of those with a T4 count <0.9x10(9)/l.

Within 4 years of infection there are significant clinical and immunological abnormalities in a heterosexual population who acquired infection via IDM despite the fact that only 40% are currently participating in a high risk activity i.e. IDM. These abnormalities are present despite the discontinuation of the high risk activity for up to 3 years in some individuals. As yet we are unable to say if progression is associated with continued IDM.

MP.138 GROWTH FAILURE IN CHILDREN WITH HEMOPHILIA AND HIV INFECTION.

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It is not known whether infection with HIV virus in children with hemophilia affects growth. As a consequence, the growth of 22 males with lymphadenopathy syndrome secondary to HIV virus and hemophilia was evaluated. 66% were below the 50th percentile for age but only 3 patients (pts) were found to have significant growth failure of 3-4 yrs duration with the onset after HIV infection. The pts were well except for lymphadenopathy; none had opportunistic infections. Height for weight was between the 25th and 50th percentiles. Results of the endocrine evaluation which included the peak growth hormone (GH) response to arginine-insulin and glucagon tolerance tests are listed.

Pt #	Age Yrs	Bone Age	Height Age	Tanner Stage	Growth Rate Cm/Yr	SmC U/Ml	Peak GH Ng/Ml
1	15.3	14	14	2	4.7	1.2	21.7
2	14.7	11.5	11	1	3.2	0.53	20.2
3	8.5	6	5	1	3.0	0.4	14.1

(Normal (nl) growth rate>5 cm/yr; nl SmC 6-11 yrs, 0.50-2.06, 12-17 yrs, 0.78-3.73; nl peak GH >10 ng/ml). All had normal thyroid function and cortisol response to insulin induced hypoglycemia. Pts 1 and 2 had mean 24 hour GH concentration (GHC) determined by measuring GH every 30 minutes (normal> 3.0 ng/ml). The GHC level was nl in pt 1 (4.95 ng/ml) and low in pt 2 (2.17 ng/ml). CONCLUSION: Growth failure in pts with hemophilia and HIV infection is not rare and does not appear to be due to classical growth hormone deficiency. In some pts, this may be the consequence of the neurodysregulation of growth hormone secretion and may be associated with hyposomatomedinemia. Further evaluation of these pts needs to be performed to determine the incidence and etiology of growth failure.

MP.139 THE SPECTRUM OF PERIPHERAL NEUROMUSCULAR MANIFESTATIONS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION.

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Peripheral neuromuscular manifestations occurred in association with HIV infection in 29 patients (12 AIDS or ARC; 17 asymptomatic HIV seropositives). Seven patients presented with a subacute polyradiculoneuropathy resembling Guillain-Barre syndrome (GBS) with decreased nerve conduction velocities and increased CSF protein (5). All seven had full functional recovery within one to six months. More than 50% of the patients with GBS seen at our institution were HIV seropositives. Twelve patients presented with a slowly progressive peripheral neuropathy manifested by increasing weakness (3), dysesthesia (4), or both motor and sensory syptoms (5). Electrophysiological studies revealed the neuropathy to be demyelinative in eight and axonal in four. CSF protein was typically increased (47-138 mg/dl). Two patients developed brachial plexitis with weakness of the serratus anterior, deltoid and the spinati and one had mononeuritis multiplex. Recurrent Bell's palsy (3) and zoster sine eruption (3) were also noted. Two patients developed a generalized myositis characterized by elevated muscle enzymes and abnormal electromyography. Peripheral neuromuscular manifestations may occur early in the course of HIV infection, long before the development of AIDS. These disorders are diverse in nature and often disabling.

MP.140 Neuropsychologic Evaluation of HIV Seropositive US Army Soldiers

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Thirty-three HIV seropositive asymptomatic soldiers identified on unit screening were staged by Walter Reed classification and assessed for neurologic disease. The 32 males and 1 female had a mean age of 28.1 and staged 7 as WR1, 23 WR2, and 3 WR3. Five patients, all WR2, had subtle neurologic findings to include slowed rapid alternating movements, upper extremity hyperreflexia, facial palsy and diminished short term memory and digit span. Ten patients had CSF IgG index by nephelometry > .75, suggesting intrathecal IgG synthesis. IgG index was not significantly different between abnormals and normal exam patients (.98±.52 vs .62±.20 p=.49). One patient each with normal exam had abnormal EEG and MRI. Nine patients had 6-13 lymphocytes/mm^3 in CSF, 2 had CSF protein 50-70 mg/dl, none had CSF/serum albumin ratio greater than .0065, and all had positive CSF HIV Western Blot when diluted 1:10. Mean WAIS-R PIQ scores were non-significantly higher in WR1 than WR2 (108.4±18.5 vs 97.7±12.7 p=.56) and in normal exam versus abnormal exam patients (101.7±14.4 vs 92.4±11.9 p=.43). Two patients had positive CSF FTA and were treated for neurosyphilis. At six month follow-up all patients remain on active duty with five of five showing mean WAIS-R PIQ improvement of ±11.6±5.8 and none showing progressive neurologic disease.

MP.141 The Importance of Clinical and Laboratory Parameters in the Management of AIDS Pneumonias

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A diagnostic bronchoscopy which was performed in 43 of 52 consecutive patients with opportunistic pneumonias in the Acquired Immune Deficiency Syndrome (AIDS) did not reveal a cause in 6. Thus there were 15 patients without a definitive diagnosis but all responded to high dose Cortimoxazole and 9 developed other signs of AIDS within six months.

In 25 of the 52 patients Pneumocystis pneumonia (PCP) was confirmed as the opportunist, but in only 3 was this by sputum induction. Cytomegalovirus (CMV) was grown from bronchial lavage specimens in 15 patients but only confirmed by transbronchial biopsy in 2. The lower the admission partial pressure of oxygen (PAO_2) the higher the diagnostic yield at bronchoscopy.

Seventy-five percent of our patients tolerated a full course of Cotrimoxazole. The mortality in patients with mixed infections (20%) was identical to that for PCP alone. Two of 5 patients in whom only CMV infection was found, and 6 of 10 patients with both PCP and CMV responded to Cotrimoxazole therapy alone.

The most potent indicator of prognosis was the admission PAO_2 (mean 9.6 KPA for survivors, and 6.7 KPA for non-survivors. ^{2} P<0.01).

Simple observations of temperature and pulse were sensitive indicators of survival. Repeated chest X-rays, blood gases and bronchoscopy did not influence the management.

MP.142 Neuropsychiatric Manifestations of Human Immunodeficiency Virus Infection: Results of an Initial Screening Evaluation of Homosexual/Bisexual Men.

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A longitudinal study of neuropsychiatric manifestations of HIV is underway in Baltimore and Chicago within the Multi-center AIDS Cohort Study. An initial screening test battery (Phase 1) is followed, in participants screening positive, by more detailed neuropsychiatric evaluation (Phase 2), and MRI, EEG, CSF analysis, where appropriate. 363 homosexual/bisexual men were screened: 158 were HIV-seronegative (SN), 157 had been seropositive (SP) > 30 months, and 48 had seroconverted (SC) during 30 months of observation. The frequency of positivity of Phase 1 screening instruments is presented:

Phase II Referral by Phase I Instrument	Chicago (Total N = 148) SP(N=83)	SN(N=48)	SC(N=17)	Baltimore (Total N = 215) SP(N=74)	SN(N=110)	SC(N=31)
Neurological Questionnaire	12 (14%)	3 (6%)	2 (12%)	6 (8%)	11 (10%)	8 (26%)
Psychiatric Sx Inventory	7 (8%)	1 (2%)	1 (6%)	14 (19%)	20 (18%)	7 (23%)
Cognitive Failures Quest.	6 (7%)	1 (2%)	2 (12%)	13 (18%)	15 (14%)	7 (23%)
Neuropsychological Tests	21 (25%)	7 (15%)	4 (24%)	8 (11%)	9 (8%)	2 (6%)
Optacon Vibration Test	-	-	-	5 (7%)	7 (6%)	2 (6%)

This preliminary analysis indicates a relatively high rate of positive screening, in all three groups, including seronegatives. Further correlation with Phase 2 testing will define the prevalence of neuropsychiatric disorders and the predictive value of the Phase 1 screen. Serial longitudinal testing of the two cohorts will delineate the incidence of neuropsychiatric disorders.

MP.143 Neurological Recovery and Prolonged Survival in Progressive Multifocal Leukoencephalopathy with HIV infection

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Pathologically confirmed progressive multifocal leukoencephalopathy (PML) was the initial manifestation of HIV infection in two individuals, a 39 year old homosexual man and 36 year old bisexual women. Both patients experienced a dramatic, though incomplete, recovery of neurological function and have survived in excess of 17 and 22 months, respectively, since the onset of their neurological symptoms. Neurological improvement correlated with improvement of abnormal immunological parameters in one patient, whereas, the other patient displayed neurological recovery despite deterioration in her immunological status and development of other opportunistic infections. An uncharacteristically intense inflammatory response for PML was observed in the brain biopsy specimens in regions where the papovavirus was detected by electron microscopy. In 13 other HIV seropositive patients with pathologically confirmed PML, progressive neurological deterioration and death within 6 months were observed. However, these two cases illustrate that PML associated with HIV infection may demonstrate neurological recovery and prolonged survival.

MP.144 Polymyositis Associated with AIDS Retrovirus

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Two homosexual men were initially seen with polymyositis as the only manifestation of the acquired immunodeficiency syndrome (AIDS) retrovirus infection. They presented with progressive proximal muscle weakness, elevated CPK and signs of inflammatory myopthy in the muscle biopsy. They developed AIDS-related complex a few weeks later and typical AIDS two to six months after onset of muscle weakness. A third patient presented with dermatomyositis having the typical skin rash on the face, around the eyes and on the chest, in addition to the other clinical and laboratory signs of inflammatory myopathy. By use of anti-human T-cell lymphotropic virus type III antiserum and monoclonal antibodies to lymphocyte subsets in an immunofluorescence technique, viral antigens were found in the OKT4-positive lymphoid cells surrounding muscle fibers and invading the endomysia septa. We conclude that an initial infection with the AIDS retrovirus can be associated with polymyositis or dermatomyositis and this may be the first clinical manifestation of an impending AIDS-related complex or AIDS.

MP.145 Progressive Neuropsychological Deficit in HIV Infection

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To determine the characteristics and prevalence of cognitive deficit in HIV infection, we performed neuropsychological (NP) assessments of 4 groups of homosexual men. 1) AIDS (N=15); 2) ARC (N=13); 3) other HIV positive (N=16); 4) seronegative (N=11). All subjects were ambulatory and none presented with clinical signs of AIDS dementia complex at time of testing.

Results. Neuropsychological abnormality was detected in 87% of AIDS, 54% of ARC, 44% of other HIV seropositive, and 9% of seronegative men. Slowed information processing was the most common finding, followed by impaired abstracting ability and defects in learning and remembering.

Conclusion. It is possible that cognitive impairment occurs early in HIV infection and may be detected even in those who do not qualify for diagnosis of AIDS or ARC.

MP.146 Regression of Oral Hairy Leukoplakia with Acyclovir

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The epithelial cells of the HIV-associated lesion, oral "hairy" leukoplakia (OHL), contain actively replicating Epstein-Barr virus (EBV). Orally administered acyclovir therapy resulted in clinical regression of OHL in 5 of 6 patients. Regression of OHL was associated with an inability to detect EBV in the area of previously recognized OHL.

A pilot study was conducted to evaluate acyclovir therapy (1.2gm/day for 20 days) in 13 HIV seropositive homosexual males with OHL involving the lateral borders of the tongue. The presence of EBV in the lesion of OHL was documented by electronmicroscopy (herpes-type particles), immunofluorescence assay (IFA) using 2 different monoclonal antibodies against EBV-VCA, in situ hybridization, and by the presence of elevated levels of EBNA-infected cells after transformation of human fetal cord blood lymphocytes upon cocultivation with OHL tissue. Adjacent uninvolved tongue had no evidence of EBV antigens by IFA or in situ hybridization. All patients had the presence of elevated levels of EBV-VCA and EA antibodies in the serum. Clinical regression of OHL occurred 14 to 28 days after initiation of therapy. After discontinuing treatment, OHL recurred in all 5 cases (range: 10-46 days). No regression of OHL was evident in the 7 untreated individuals after 6 months of follow-up. Regression of OHL was associated with an inability to detect EBV by IFA and in situ hybridization in the previously involved area of OHL. It appears that EBV infection and replication is directly responsible for the clinical lesion of OHL. Acyclovir therapy inhibits the replication of EBV resulting in regression of the OHL lesion.

MP.147 "False-Positive" Antibodies to Human Immunodeficiency Virus (HIV) Detected by an Enzyme-Linked Immunosorbent Assay (ELISA) in Patients at Low Risk for Acquired Immune Deficiency Syndrome (AIDS)

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ELISA testing for anti HIV antibodies using the Abbott© kit was performed on 290 sera from patient from 2 groups: (1.) at high risk for or having symptoms of HIV infection and (2.) at low risk for HIV infection (231). Group 2 included patients with non HIV related immune deficiencies, dermatologic, neucologic, collagen vascular or hematologic disorders.

25 patients had high absorbancy ELISA results (>1.0 absorbance units). All of these patients had positive Western blot (immunoblot) analyses and were all in Group 1. 20 patients had moderate or low ELISA results (≤1.0 absorbance units). 2 of these 20 patients had positive Western blots and were in Group 1. The remaining 18 patients were in Group 2. 8 of these had chronic liver disease, 4 had multiple myeloma and 6 had various disorders. These 18 patients presumably had "false positive" reactions for HIV using this ELISA test.

MP.148 Lymphoid Interstial Pneumonitis (LIP) in HIV-I or HIV-II infected patients.

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Eleven adult patients [9 male, 2 female ; haitian (7 cases), african (3 cases), caucasian (1 case) were] investigated for interstial pneumonitis. In 10/10 cases, lymphocyte count was increased (>140 x 10^3/ml) in broncho-alveolar lavage fluid and in 4/5 cases more than 80 % of the lymphocytes were T_8^+. No pathogens were isolated. In 5 patients, open lung biopsy showed the histological picture of LIP. Ten patients had persistent generalized lymphadenopathy (PGL), and the caucasian patient had AIDS. Blood T_4-cell count were decreased (≤ 600/ml) in all patients. HIV I-IgG antibodies were detected in 9/11 patients. The homosexual caucasian man lived in Mauritania ; he showed IgG antibodies to HIV-II.

During a mean follow-up time of 30 months (9-36), 3 patients had recurrent bacterial infections ; their frequency decreased by use of I.V. gammaglobulin in 2/2 cases. Four PGL patients developed opportunistic infections. The HIV-II infected caucasian patient died of a high-grade lymphoma with lung involvement.

Lung is a pulmonary manifestation of HIV-I or HIV-II infection. LIP seems to be more frequent in black patients.

MP.149 Isolation of HIV from cerebrospinal fluid of patients with AIDS related disorders.

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We evaluated biological involvement of CSF by HIV in a prospective study by viral culture (reverse transcriptase activity) in the CSF of 10 preAIDS patients (Walter Reed classification), 13 AIDS without neurological symptoms, 10 preAIDS and 10 AIDS with neurological symptoms. HIV was isolated in the CSF in 15 patients without pleiocytosis (<15 cells/mm3), and was correlated to viremia (13/15) Presence of HIV in the CSF is related to the general status (10/23 AIDS), or to the neurological involvement whatever the symptoms (9/20 AIDS and preAIDS). Only 1 preAIDS (WR5) without neurological symptoms was positive, all the other preAIDS patients were negative (5 WR2, 3 WR3, 1 WR4). Glycoprotein antibodies were found in the CSF in all patients by Western blot analysis (gp110, gp160). Intrathecal synthesis of antibodies was evaluated by ELISA and did not have a discriminating value. Presence of the virus in the CSF should be investigated prior to any evaluation of an antiviral drug since a failure could be due to a silent neurological involvement (6/23 without neurological symptoms).

A greater cohort of preAIDS patients is being evaluated and repeated lumbar puncture data will be provided o establish a correlation with CT scans, general and neurological prognosis.

MP.150 Psychiatric Consultation to AIDS Patients, 1981-1986: A Consultation Liaison Perspective

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The psychiatric morbidity associated with Human Immunosuppressive Virus (HIV) infection reflects varied biopsychosocial etiologies and may require adaptations in the provision of consultation services. The psychiatric care of AIDS patients was evaluated by reviewing all service consultations to AIDS and ARC patients between 1981 and 1986 at St. Luke's Hospital, a 776-bed teaching facility in New York. Specifically, these were evaluated in terms of reasons for consult requests, time between admission and consultation, number of psychiatrist's visits, psychiatric diagnosis, and treatment. The data were compared to similar data for all general hospital patients consulted by psychistry in the same years.

In the 5 year study period, the number of consultations to HIV patients increased 17-fold. The most common psychiatric diagnoses were adjustment disorders (24%) and organic brain syndromes (24%). Neuroleptic medication was used frequently (28%). There were also variations in the treatment of patients in different risk groups.

Compared with general hospital patients, reasons for requesting consultations were similar (principally depression, suicidal ideation, and treatment refusal) although HIV patients required 1/3 more visits than did general medical patients. Differences were also observed in the distribution of psychiatric diagnoses and in the provision of suicide precautions.

The evaluation of psychiatric consultation data provides clinicians with a way to gauge the effect of AIDS on psychiatric services. Furthermore, it offers measures of the psychosocial morbidity and clinical needs associated with AIDS.

MP.151 Absence of Correlation Between Serological Results, Neutralizing Antibody Titers, and Progression of HIV-related Disease

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We reviewed serologic and neutralization antibody data on 50 random HIV seropositive patients to determine whether any serological markers of clinical outcome existed. At the time of initial specimen acquisition, 20 subjects were asymptomatic or had HIV-related diseases but not AIDS. Eight had KS and 22 had prior opportunistic infections with or without KS. The major serologic change over time was the loss of the p24 antibody band. Eight of 11 subjects with this pattern had had opportunistic infections. Patients with and without the p24 band initially had similar rates of development of KS or new opportunistic infections, and when loss of the band was seen, it usually occurred after the onset of opportunistic infections. Serial ELISA titers were done on 31 subjects. Eight of 31 had at least a four-fold fall in titer over the period of observation. Only 2 of 8 had the fall in titer before the development of opportunistic infections. Five had a decline in titer after disease progression and 1 was clinically stable despite the decline. Similar results were seen with titer of immunofluorescent assays. Neutralization activity was measurable in 30 of 31 subjects at titers of 1:4 to 1:128. Titers were stable over time and there was no correlation between neutralization titer and initial diagnosis or eventual progression of disease. Utilizing current serological techniques and serial specimens, we find that changes in HIV antibody titer and immunoblot pattern are insufficiently sensitive and specific to predict course of disease. Similarly, neutralizing antibody titer is not a good prognosticator of disease progression.

MP.152 Salivary Gland Function in Early AIDS Patients

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Saliva plays a primary role in modulating oral microbial colonization patterns. Reports of xerostomia and oral candidiasis in AIDS patients suggest the possibility of altered salivary gland status. The purpose of the present study was to assess salivary gland performance in early diagnosed AIDS patients. All patients were homosexual or bisexual males, HIV culture positive ± cutaneous Kaposi's sarcoma and/or lymphadenopathy. Patients were divided into two groups; those being treated with AZT and others who had received no treatment. Two control groups were used: healthy men and male patients with complaints unrelated to salivary glands. Parotid and submandibular/sublingual salivas were collected on ice and stored at -70° until analysis (volume, Na^+, K^+, Cl^-, total protein, albumin, lysozyme). There were no marked differences found between AIDS ± AZT patients and the non-AIDS control groups with respect to electrolytes, total protein and salivary flow rates, for parotid and submandibular/sublingual glands under both basal and stimulated conditions. However, the frequency with which albumin was observed in saliva of both AIDS groups was dramatically increased; being seen in 48/73 AIDS saliva samples but in none of the 64 control samples. Albumin in gland saliva indicates the loss of salivary epithelial integrity. Also both AIDS groups had 2-3 fold higher levels (than controls) of lysozyme, an antimicrobial protein secreted by salivary ductal cells. The data demonstrate (1) early-diagnosed, metabolically stable AIDS patients show evidence of specific salivary gland dysfunction and (2) AZT therapy has no effects on salivary performance. These results suggest that study of salivary antimicrobial factors will be important with respect to the development of oral opportunistic infections.

MP.153 Natural history of HIV-1 infection in children.

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To investigate the natural history of perinatal HIV-1 infection we studied babies born to mothers belonging to high risk groups. Fifty eight infants and children born to HIV-1 seropositive mothers have been studied over the last two years. Blood samples were obtained at birth or in the first six weeks of life in 45 cases. All babies were evaluated serologically, virologically, and clinically every two months; neuromotor assessment and evaluation of mental development were also performed. Sera collected at birth or in the first six weeks of life from 45 babies were positive for IgG specific antibodies: however 30% of babies older than six months became seronegative. Cultures from peripheral blood lymphocytes, tested for reverse transcriptase activity, were negative in all seronegative children; cultures derived from 9 out of 25 seropositive children, older than six months, were positive in the reverse transcriptase assay.

Two infants had AIDS and 7 AIDS-related complexes. To date the other babies younger than 18 months are clinically well and laboratory data are in normal range. In most of the older asymptomatic children T4/T8 ratios are < 1.0. Although some babies received live oral polio vaccine and/or are shedding Cytomegalovirus in the urine, none of them present clinical signs of infection due to these viruses. Neurological development is normal in all asymptomatic infants while mental evaluation is in progress.

MP.154 Human immunodeficiency virus (HIV) -related polyradiculoneuropathy (PRN) : lack of evidence for antiperipheral nerve antibodies (PNA).

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Five patients (pts) who presented with flaccid paraparesis and high cerebrospinal fluid (CSF) HIV antibody level were investigated in evolutive phase. Four of these pts met the criteria of AIDS. Clinical picture consisted of progressive distal and symmetrical weakness, with abolished reflexes. Mild sensory impairment was present in 3 pts and absent in 2 pts. Nerve conduction velocities were slowed in 3 pts. CSF protein was elevated (mean 364 mg/dl) and white cells were 2 to 109/mm^3. Sural nerve biopsy performed in 3 pts showed segmental demyelination with intact axons and no inflammatory cells infiltration in 2 pts and was normal in 1 pt. Intrathecal synthesis of HIV antibodies was found in 3 pts and CSF culture was positive for HIV in 1 pt. All pts displayed polyclonal hypergammaglobulinemia. Except for HIV infection, other causes of PRN were excluded. The presence of circulating PNA was investigated by incubating normal nerve with pts'serum and CSF then with FITC-conjugated antibody to IgG, IgM and IgA. No binding was observed. The presence of immunoglobulin deposits in sural nerve biopsy was investigated in 3 pts by immunostaining with FITC-conjugated antibody to IgG and IgM. No deposits were observed.

These data suggest that the pathogenesis of HIV-related PRN is not mediated by PNA.

MP.155 Analysis of Bacteremias in Patients with AIDS.
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Bacterial infections may cause significant disease in patients (pts.) with AIDS. To explore this issue, we studied bacteremias (Bs) occurring in a well-defined AIDS population. Microbiology records at Montefiore Med. Ctr. (MMC) and N.Central Bx Hospital (NCB) were reviewed for all significant Bs occurring between 1/82 and 7/86. Bs were cross-referenced with a registry of pts. with AIDS hospitalized during this time. Available records for these pts. were reviewed. Sixty-nine Bs occurred in 58 of 306 (19%) AIDS pts. for a rate of 22.5 Bs/100 AIDS pts. At MMC during this period 2,244 Bs occurred in 83,955 pts. without AIDS for a rate of 2.7 Bs/100 pts. ($p<0.05$). The occurrence of B among pts. with AIDS was not significantly associated with risk group, age, gender or race. However, B due to S. aureus was significantly more common in pts. with intravenous drug use as their heirarchical risk behavior for AIDS ($p<0.05$). Organisms most frequently causing B included S. aureus (21 episodes) S. pneumoniae (12), salmonella sp. (12), P. aeruginosa (7) and other gram negative bacilli (13). Six episodes were polymicrobial. Twenty-six of 54 (48%) evaluable Bs were community acquired, 22/54 (41%) were nosocomial (70% of S. pneumoniae were community acquired, 69% of S. aureus nosocomial), and the remainder could not be classified. Eighty percent of B occurred at or following the diagnosis of AIDS (78% of community acquired, 96% of nosocomial). In 45% of patients with B, the infection causing B was the reason for admission. Survival analyses revealed no significant shortening of life expectancy among AIDS pts. with B.

We conclude that AIDS pts. are at significantly increased risk for B regardless of risk group or other demographic variables. Therefore, the increased rate of Bs in AIDS pts. is likely the result of HIV infection. Although Bs are frequent among AIDS pts. they do not appear to significantly influence survival when appropriately diagnosed and treated.

MP.156 Pregnancy Outcomes and HIV Infection in Intravenous Drug Abusers
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Beginning 7/1/85 we studied the effect of HIV infection on outcome of known pregnancies in intravenous drug abusers attending a NYC methadone program. Both seropositive (SP) and seronegative (SN) women enrolled in a prospective study of HIV infection were monitored for early pregnancy with monthly urine testing. Additional women were tested for HIV serum antibody (Ab) after conception. Obstetrical and infectious complications were monitored and serial HIV Ab and T-cell studies performed. Among women not pregnant at the time of initial HIV Ab testing, 12/71(17%)SPs vs.19/145(13%)SNs became pregnant over 18 months of follow-up. Among pregnant women informed of HIV Ab status ≤24 weeks gestation, 4/10(40%) SP vs. 6/17(35%)SN elected to terminate. 33 pregnancy outcomes occurred in 26 SPs without AIDS or oral thrush (mean age 30), and 45 outcomes in 44 SNs (mean age 29).

	Number of Outcomes	Spontaneous Abortions	Ectopics	Elective Terminations*	Livebirths ≤37 weeks	Livebirths >37 weeks
SPs	33	3(9%)	0	14(43%)	3(9%)	13(39%) *p=NS
SNs	45	2(5%)	2(5%)	11(24%)	7(16%)	23(50%)

Of 44 women carrying >24 weeks (15SP,29SN), mean third trimester hemoglobin levels (11.4 vs. 11.5) were not different. SP women had lower lymphocyte counts (1769 vs. 2319) and T-cell ratios (0.88 vs. 1.65, $p<.05$). 5/15(33%) SPs were hospitalized for infections; gastroenteritis(2), pneumonia(2), cellulitis(1),vs. 2/29(7%) SNs; gastroenteritis(1), pyelonephritis(1), ($p<.07$). The frequency of other medical and obstetrical complications during pregancy or at delivery did not differ between the two groups. There were no differences in self-report of drug abuse during pregancy.

HIV Ab was not associated with a decreased occurrence of pregnancy in SPs, nor with early or late adverse pregnancy outcomes. Data suggest that pregnant SP women may be at increased risk of serious infectious complications. Frequency of elective termination was not significantly increased in SP women. These findings have important implications regarding perinatal transmission of HIV infection.

MP.157 ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) ASSOCIATED RENAL DISEASE: A LONGITUDINAL ANALYSIS.
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Over a four year period between 1982 and 1986, among 800 patients with AIDS seen at two urban institutions, 95 were evaluated for renal abnormalities consisting of varying degrees of azotemia, proteinuria and hematuria. We classified renal disorders in AIDS on the basis of clinical presentation, hospital course, and renal histology (when available). There were 23 patients with potentially reversible acute renal failure (ARF); 54 patients with AIDS associated nephropathy (AAN); and 18 patients who developed AIDS while undergoing maintenance hemodialysis (AIDS-MH) (Table).

YEAR	ARF		AAN		AIDS-MH
	Cr<6	Cr>6	Cr<6	Cr>6	
'82	0	0	0	2(2)	1(1)
'83	2	1(1)	2	9(7)	0
'84	1	8(4)	4	9(7)	4(4)
'85	1	1(0)	0	9(3)	6(6)
'86	2	7(1)	4	15(12)	7(7)
TOTAL	6	17(6)	10	44(31)	18(18)

Number ( ) represents pts dialyzed

Among the ARF group, 6 of 17 with serum Cr>6 mg/dl who were dialyzed, 5 recovered sufficient renal function and survived without further dialysis for a median 17 months. In the AAN group, 44 of 54 patients developed irreversible uremia, and 31 were repeatedly dialyzed. Median survival of dialyzed AAN patients was 1.4 months. In the AIDS-MH group, all 18 patients were IV drug addicts, who developed AIDS within 7 months (median) of initiating maintenance hemodialysis. Their median survival after diagnosis of AIDS was 1 month despite dialysis. From these data we conclude that renal failure both acute and chronic in AIDS is increasing and survival continues to be very poor.

MP.158 Hypoxemia and neutrophilic alveolitis as prognostic factors of Pneumocystis carinii pneumonia (PNC.C.P.) in HIV infected patients.
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This study concerns 46 HIV infected patients (pts) with PNC.C.P. and without identifiable associated infection. At the time of diagnosis of PNC.C.P., PaO_2 and BAL data [total cells, number and percentage of lymphocytes (L) and neutrophils (PMN)] were evaluated. All pts were treated with Trimethoprime-Sulfamethoxazole (TMP-SMZ) ; they were divided into 2 groups, according to the evolution of their pulmonary disease (G I : 10 with fatal acute respiratory failure ; G II : 36 with a favorable outcome).

The significant correlations between initial PaO_2 and/or BAL data (cell count/mm^3 - G I 107±77 ; G II 189±120) and evolution are indicated in the following table.

G	Nb pts N	PaO_2 mm Hg	PMN %	PMN/L	PaO_2 <50 n pts/N	PMN >5/mm^3 n pts/N	PMN/L> 0.5 n pts/N
I	10	52 ± 13	26 ± 26	0.57 ± 0.9	7/10	9/10	7/10
II	36	67 ± 19	10 ± 13	2.9 ± 4.2	8/36	18/36	10/36
		$p<0.02$	$p<0.05$	$p<0.001$	$p<0.01$	$p<0.03$	$p<0.01$

It is to be noticed that : 1)There is a significant relation between PaO_2 and PMN (%) and 2)Post-mortem examination of lung from 8 G I pts showed fibrosis in 7 cases.

Conclusion : Initial $PaO_2<50$ mm Hg and PMN/L (in BAL)>0.5 were present in 5/10 pts of G I. Even though this association was also present in 4/36 pts of G II, it seems a poor prognostic factor and, when present, probably indicates that other initial treatment, e.g. a TMP-SMZ/steroid association, should be considered.

MP.159 Progressive Multifocal Leukoencephalopathy (PML) in AIDS Patients: Diagnostic Considerations and Pathologic Findings.
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PML, a subacute demyelinating disease due to JC virus (JCV), is seen frequently in AIDS patients. We have previously reported the use of in situ hybridization with a biotinylated JCV probe in the diagnosis of PML. Three AIDS patients with PML have been studied with this technique on either brain biopsy or autopsy tissues. In one patient, the diagnosis of PML was established within 4 hours of biopsy by in situ hybridization performed on frozen sections using a modified technique developed by one of us (EM)). Formalin-fixed biopsy tissue confirmed these findings. Areas of demyelination associated with JCV infection of oligodendrocytes, and astrocytosis were found throughout the biopsy. In another patient, areas of demyelination found in biopsy tissue had none of the other pathological features of PML In situ hybridization with the JCV probe demonstrated infection of oligodendrocytes, which confirmed the diagnosis of PML. Autopsy studies in two patients revealed extensive demyelination in the white matter of the cerebral hemispheres. In one, JCV infected cells without other pathologic changes were found scattered throughout the cerebral hemisphere and PML lesions extended into the cerebral cortex. Our studies suggest that PML in AIDS patients is often more extensive and histological changes may be more subtle than when the disease occurs with other immunosuppressive illnesses. The use of in situ hybridization is essential in rapidly establishing the diagnosis of PML in patients with AIDS.

MP.160 The Need for Tissue Diagnosis of Central Nervous System Lesions with the Acquired Immunodeficiency Syndrome.
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Patients with acquired Immunodeficiency Syndrome (AIDS) who have central nervous system (CNS) lesions and positive toxoplasma serology are often presumed to have cerebral toxoplasmosis and are treated accordingly.

We examined records for 600 AIDS patients retrospectively and found 47 with CNS lesions on CT scan. Lesion types included multiple and single ring enhancing as well as multiple and single hypodensities. Nineteen of these patients had positive toxoplasma serology. Of the thirteen with brain biopsies, 6 had toxoplasmosis, 2 had tuberculosis, 2 had encephalitis of unknown cause, 1 had nocardia and salmonella, 1 had vaccuilitis and 2 showed nonconclusive results. Biopsies of 3 of the patients with significant toxoplasma serology showed no evidence of toxoplasmosis.

The majority of the cases (36) had been presumptively diagnosed as having toxoplasmosis and treated with anti-toxoplasmosis regimen--pyrimethamine and sulfadiazine (30) or pyrimethamine and trimethoprim-sulfamethoxazole (6).

That 8 of the 13 biopsies revealed diseases other than toxoplasmosis, some of them treatable, suggests that other diseases may be common and that biopsies of CNS lesions in AIDS patients are needed to make accurate diagnoses to detect treatable diseases and to avoid unnecessary treatment.

MP.161 Sclerosing cholangitis in AIDS

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Cholangitis was documented in 6 out of 101 AIDS patients (pts) whose liver histology was available (surgical biopsy:1, needle biopsy:53, autopsy:68). Right hypocondrial pain and prolonged fever were present in 4 patients. Anicteric cholestasis occurred in all patients and was major in 4 (alkaline phosphatases : 8 x normal value). Diagnosis was made by endoscopic retrograde cholangiography and laparotomy (1 pt), needle biopsy (2 pts) and/or autopsy (4 pts). Sclerosing cholangitis associated with pericholangitis predominated on proximal intrahepatic biliary ducts. In 5 cases, numerous typical cytomegalovirus (CMV) inclusions were present in both biliary epithelium and endothelial cells. In one case, no intra-hepatic biliary duct inclusions could be found at autopsy although CMV cholecystitis was present. All patients had CMV viremia and disseminated CMV infection ($\geq$ 2 organs). These data show that cholangitis occurs in 6% of AIDS patients and is one of the multiple factors involved in the frequent cholestasis. Needle biopsy could underestimate its prevalence because of the predominant proximal biliary duct involvement. Cholangitis is mainly due to CMV but can also occur without any opportunistic agent as already reported in other immunocompromised status.

MP.162 Children's Hospital AIDS Program (CHAP): I Demographic and Clinical Data 1984-1986

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Sixty three children with symptomatic HIV infection were enrolled in CHAP from 1984-1986. 46% AIDS; 54% ARC. Male:female ratio 0.85:1. Ethnic origin distribution: Black 52%; Hispanic 24%; White 21%; Haitian 3%. Risk factors: mother IVDU 40%; mother sexual contact of IVDU 30%; both parents IVDU 10%; neonatal transfusion 6%; maternal transfusion 5%; hemophilia 3%; Haitian 3%; multiple risk 1.5%; unknown 1.5%. Excluding hemophiliacs, mean age at enrollment was 1.88 yrs (0.2-7.75); 11/61 were enrolled at >4 yrs. 16/63 (25%) of patients were first seen to be screened for HIV because of known risk: 8/16 were healthy; 8/16 had chronic symptoms; 35/63 were first seen for acute illness. Among these 63 children, signs and symptoms over 2 yrs included: rash 95%; lymphadenopathy 92%; hepatosplenomegaly 87%; fever 84%; respiratory findings 79%; thrush 71%; encephalopathy 68%; FTT 56%; recurrent otitis media 49%; abdominal distention 48%; diarrhea 43%; clubbing 21%; gingivostomatis 19%; parotitis 11%; abdominal pain 11%; CHF 8%; epistaxis, joint pain, conjunctivitis, GI bleeding, jaundice <5%.

There were 23 opportunistic infections (8 PCP, 8 Candida, 2 Toxoplasmosis, 3 disseminated CMV, 1 disseminated adenovirus, 1 MAI); 4/63 had neoplastic disease (1 CNS lymphoma, 1 GI leiomyosarcoma, 2 pulmonary lymphoproliferative disease). 29 episodes of bacterial sepsis occurred; 20 streptococcal; 4 Salmonella spp.; 3 H. influenzae; 2 S. aureus. LIP/OIP was documented in 23/63 (57%) of children. HIV is a chronic multisystem disease with protean manifestations. The practitioner must maintain a high index of suspicion for HIV infection in children.

MP.163 DETECTION OF INFECTIOUS HUMAN IMMUNODEFICIENCY VIRUS (HIV) IN SEROPOSITIVE INFANTS AND CHILDREN

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While the majority of children infected with HIV develop antibody, a significant number may have undetectable infectious HIV in their peripheral mononuclear cells (PMC). We evaluated 26 seropositive children for the presence of infectious HIV in their PMC and assessed in vitro immunologic parameters and clinical status. Of the 13 seropositive, culture negative children, 6 acquired their infection from infected mothers, 2 from blood transfusions, and 5 from factor VIII/IX transfusions. Normal T and B cell immunity were found in 8 out of 13 and 11/13 were clinically well. In contrast, of the 13 children who were seropositive, culture positive (5 maternal transmission, 4 blood transfusion, 4 factor transfusion), all (13/13) had abnormal T cell and B cell immunity. Of the 13, 12 had AIDS or ARC and 2 have died. In 10 of the seropositive, culture negative children followed prospectively there has been no significant disease progression. In 4 seropositive, culture positive children detectable virus was associated with clinical and/or laboratory deterioration. Our results suggest that in seropositive children the presence of detectable HIV in PMC correlates with severity of laboratory and clinical evidence of disease and may be an important prognostic factor.

MP.164 DIFFUSE CERVICAL CELLULITIS ASSOCIATED WITH HIV 1 INFECTION IN CENTRAL AFRICA.

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Within a seven month period ten cases of diffuse cervical cellulitis have been observed in the stomatological department of Bangui general hospital. All of them resulted from non-treated dental infection.

Clinical symptoms showed emphysematous gangrene and large facial necrosis. Bacteriological examination of pus withdrawn by syringe under anaerobic conditions allowed us to identify in one case Fusobacterium nucleatum and in two cases Clostridium perfringens, while no consistant interpretation was possible in seven cases. Nine of ten patients were HIV 1 antibodies carriers (ELAVIA and Western Blot) without any other symtom of confirmed AIDS.

We consider acute diffuse cervical cellulitis as a possible first symptom of an A R C in HIV 1 positive patients, in Africa.

In this syndrom (ARC), treatment consisting of large surgical debridement associated with penicillin and metronidazole therapy, has always been efficient.

MP.165 Asymptomatic Neurologic Infection in Persistent Generalized Lymphadenopathy Syndrome Associated to HIV Infection.

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We searched by ELISA and Western blot techniques antibodies to HIV in serum and CSF of 40 patients with PGL.All were intravenous drug addicts and none presented neurologic manifestations.All CSF analyzed were free from red blood cells.In 10 patients (25%) we found antibodies to HIV in serum and CSF by both methods.Results are listed in the following table:

Patient No	ELISA CSF	WB CSF							ELISA Serum	WB Serum						
		p18	p24	p33	p41	p55	p68	p110		p18	p24	p33	p41	p55	p68	p110
1	+	-	-	-	-	+	+	-	+	±	+	-	+	+	+	-
2	+	-	+	-	+	+	+	-	+	-	+	-	+	+	+	-
3	+	+	+	-	+	-	-	-	+	-	+	-	+	+	+	+
4	+	+	+	-	+	+	+	-	+	-	+	-	+	+	+	-
5	+	-	-	-	+	-	-	-	+	-	+	-	+	-	-	-
6	+	-	+	-	+	+	+	-	+	-	+	-	+	+	+	-
7	+	-	-	-	+	-	-	-	+	-	+	-	+	+	+	-
8	+	+	+	-	+	-	-	-	+	+	+	-	+	+	-	+
9	+	-	-	-	+	-	-	-	+	+	+	-	+	-	+	-
10	+	+	±	-	±	-	-	-	+	+	+	-	+	-	-	+

Leakage of HIV-specific antibodies from the serum to the CSF can not be excluded nevertheless immunoglobulins do not diffuse substantially into the CSF in the absence of brain or meningeal inflammation, what leads us to assume that these patients present asymptomatic CNS infection.Asymptomatic neurologic infection may be an early event in HIV infection.Follow-up may confirm our findings.

MP.166 Development of antigen and antibody titers against various HIV-antigens in the course of HIV-infection

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Prognostic significance has been attributed to the presence and titer of HIV core and env antibodies. For this study, we analyzed sera from HIV-infected persons with different manifestations of the disease for the presence of HIV core antigen, and env antigen. We used the Abbott antigen EIA and HTLV-III antibody confirmatory EIA to test for env and core and the Behring ELISA for whole virus.

Healthy HIV-infected persons exhibit relatively high anti-core antibodies. With the development of LAS and AIDS the median antibody titers decrease as well as the overall percentage of positive persons. A trend to a transient increase of anti core titers has been observed in ARC patients. Most AIDS patients are negative for core antibodies. The lack of core antibody is usually associated with the presence of HIV antigen. In contrast, there are no remarkable changes of the usually high env-antibody titers during the process of disease development. These data indicate that the combined use of different HIV tests in HIV-infected persons during the course of disease development can be of prognostic value.

MP.167 Dysmorphic Features in Children HIV Positive

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The majority of children infected by HIV are born to HIV positive mothers. Transmission of HIV may occur: early intrauterine; during materno-filial lymphocytary transfusion; during or after delivery.

Recently Marion et al. described an embryopathy probably caused by the first mechanism of transmission. We have studied the morphological features of 22 children HIV seropositive, aged between 3 months and 3 years; 11 males and 11 females. All of them were born to intravenous drug abusing and/or prostitute women, HIV seropositive. The HIV antibodies were tested by both ELISA and IFI.

The dysmorphic features found were: Growth failure 40% (Height and weight less than the third percentile for chronologic age); microcephaly 20% (HC less than 10th percentile); prominent forehead 45%; flattened nasal bridge 77%; long palpebral fissure 86%; blue sclerae 81%; obliquity of the eyes 36%; triangular philtrum 77%; marked and cleft prominence of the mental protuberance 59%; epicanthus 40%; low-set malformed ears 45%; markedly patulous lips 31%; simian creases 22%; horizontal and deep flexion creases in palms 31%; clinodactyly 9%.

Not all children were equally affected with these dysmorphic features. The most characteristic alterations affected to eyes and eyelids (86%). These percntages are significative higher than those of children born to mother of risk-group but HIV seronegative. Neither intraocular nor cardiac stigmata were found. None mother was alcohol abuser. No other intrauterine infections were demonstrated but one by CMV.

We confirmed, in our area, HIV associated embryopathy which also affected to the hands and feet.

MP.168 Clinical Patterns Emerging from Longitudinal Study of Australian Haemophiliacs with HIV Antibodies.

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HIV-ELISA confirmed by Radioimmunoprecipitation or Western Blot showed in 1984/85 a seropositive rate of 45% overall in a representative group of 161 Haemophiliacs from New South Wales. Retrospective analysis of the sera of this population using ELISA and Western Blot has now established that HIV antibodies were detectable as early as 1981.
Serial monitoring of the clinical status and T cell subsets of these patients since 1984/5 and a subgroup of them since 1983 has revealed that almost all the HIV Ab^+ patients have followed one of the patterns :
A: Decline in $CD4^+$ cells associated with a fall in CD4:CD8 ratio (14%)
B: Persistent low $CD4^+$ or CD4:CD8 ratio (25%)
C: Rising level of $CD4^+$ or CD4:CD8 ratio from a low baseline (8%)
D: Normal T cell subsets and ratio (39%)
E: Wide fluctuations in T cell subsets in the absence of a precipitant(14%)
Three patients (33%) with pattern "A" ,one with pattern "B" and one with pattern "E" have developed symptomatic immunodeficiency with three fatalities to date. Occasional episodes of autoimmune disease have occurred in patients with patterns "B" and "C" but none of these individuals has developed symptomatic immunodeficiency.
Whilst the very long term prognostic significance of these patterns occurring in the five years after infection has yet to be determined this data indicates that markedly abnormal T cell ratios may commonly persist in HIV exposed Haemophiliacs without an adverse short term outcome.

MP.169 Spectrum of HIV Infection in Neonatal Recipients of Blood Products

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Neonates who received blood products from multiple donors prior to blood bank screening represent a population at risk for HIV infection and may have a different presentation than infants at risk through vertical transmission.

We have tracked 56 neonates who received 60 blood products gleaned from 7 donors who were later found to have AIDS/ARC/sero-positivity; 4 neonates each received products from 2 high risk donors. Two additional neonates received multiple transfusions resulting in AIDS but no high risk donors were identified. Of the 60 products generated, only 1 donation occurred following the institution of voluntary donor deferral in 1983.

Fourteen patients had died prior to study, including 11 who died during their initial admission. HIV infection could have played a role in 6 of these infants who lived 5 to 15 months after the implicated transfusion and who subsequently died of infectious causes.

Forty-four infants were available for further study. 14/16 infants tested are infected with HIV. 5/14 died of AIDS 1-4 years after transfusion. 8/14 are living with AIDS/ARC at 4-6 years, including 4 in whom the diagnosis was not considered until antibody screening was performed. One patient is sero-positive but well at 7 years. Only 2/16 screened were sero-negative despite an interval of up to 7 years between time of donation and confirmation of infection in the donors. Of the 28 patients remaining, 14 have been located and study visits are pending and 14 have not been located to date.

Large numbers of neonates may have been infected with HIV prior to effective screening programs. A spectrum of disease due to HIV infection in pediatric patients should be stressed as this diagnosis had not been considered in 5/14 of our infected children in spite of significant symptoms in 4 of them.

MP.170 Arteriopathy in Children with AIDS

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Pathologic features with special reference to arteries of different organs (heart, lungs, kidneys, spleen, intestine, brain etc) seen at autopsy in six children with Acquired Immune Deficiency Syndrome (AIDS) are described. Small and medium size arteries which were most commonly involved showed: a) intimal fibrosis, fragmentation of elastic tissue, fibrosis and calcification of media variable luminal narrowing and b) vasculitis/perivasculitis. In one case, aneurysms of the right coronary artery with thrombosis and myocardial infraction were seen. Vasculitis/pervasculitis seen only in the brain may be related to the agent associated with AIDS encephalopathy. The fibrocalcific arterial lesions resemble Infantile Arterial Calcification of Infancy most closely but because of differences in age incidence, clinicopathologic and immunologic features and size and distribution of involved arteries, the arterial lesions of pediatric AIDS appear to constitute a distinctive arteriopathy. Infection(s) secondary to immunodeficiency resulting in increased exposure to endogenous and exogenous elastases may be related to pathogenesis. Role of HIV cannot be entirely ruled out. Luminal narrowing from the arterial lesions may be related to atrophy, cell depletion, scarring and necrosis/infarcts of different organs in children with AIDS. Pediatricians should be alert to the possibility of arterial involvement in pediatric AIDS.

MP.171 WELSH AIDS CAMPAIGN

GEORGE, ALAN M* and GRIFFITHS, C**; Welsh Office*, Cardiff United Kingdom, and Welsh AIDS Campaign**, Cardiff.

This Campaign is an attempt on a country-wide basis to establish an organisation to tackle AIDS as a community, behavioural, social and educational problem rather than a medical one. The Campaign is funded by the Government but is independent of it.

The aim is to provide up-to-date information for the public and professionals; to modify personal behaviour; to alleviate anxiety; to train volunteers, health educators and professionals; to provide advice to individuals and groups and to promote consistency in the message on AIDS presented by the media and others working in the AIDS field.

It is thought to be the first project of its kind in a European country and will thus be of interest to people in other countries including the United States as considerable help was obtained from colleagues in New York and New Jersey in establishing the Unit.

The demonstration will show in detail the programmes developed for use in schools, with voluntary workers, health professionals and intravenous drug abusers. The resources produced to meet the needs of these groups as a result of the above programmes will be shown.

An evaluation programme is running concomitantly.

MP.172 AIDS on Campus: Strategies for Response

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The social and political impact of AIDS creates a complex epidemic with far reaching economic and psychosocial concerns for the health care and education systems. The School of Allied Health Professions, SUNY at Stony Brook has responded to the crisis through a community service project, and two major educational projects. The community service project provided an information and referral hotline as well as community educational and service activities. That project is now a free-standing agency in the community. The SUNY AIDS Education project is designed to reduce the fear and anxiety of AIDS in college students. A comprehensive curriculum was developed and field tested during the first year of the project and is being implemented on 50 of the 64 campuses of the university and community college system. The implementation phase included a training session for campus facilitators and an evaluation plan for the program. These projects were funded by the New York State Department of Health, AIDS Institute.

The School of Allied Health Professions has been awarded a training grant from the National Institute of Mental Health to develop an AIDS resource center. This project will include faculty development, student education, in-service education, and provide consultative services and a quarterly newsletter.

A discussion of these projects, their impact on the School and University in relationship to policy decisions will allow educators and health care administrators to explore strategies for influencing institutional responses to AIDS on the college campus and in health science centers in regard to students and employees.

MP.173 The Application of Social Marketing Principles to AIDS Prevention and Education Programs: Implications and Considerations drawn from a Worldwide Survey

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Social marketing is the design, implementation, and control of programs seeking to increase the acceptability of a social idea or cause in a target group. It utilizes concepts of market segmentation, consumer research, concept development, communication, facilitation, incentives, and exchange theory to maximize target group response. Synonymous terms might be "social cause marketing," "idea marketing," or "public issue marketing."

Social Marketing, as the application of basic marketing principles to generate a social benefit, has proven its effectiveness in a number of family planning programs, particularly the retail sale of contraceptive products especially in the developing countries. Social Marketing International Association, a professional membership association based in Mexico, decided to research the feasibility of applying this experience together with basic marketing principles to prevention programs designed to reduce the transmission of HIV. Six countries were chosen for case study presentation: the U.S., U.K., Brazil, the Philippines, Zaire and France. Case study presentations of all country situations will be within the following seven point framework: 1) problem definition, 2) goal setting, 3) target market segmentation, 4) consumer analysis, 5) influence channels analysis, 6) marketing strategy and tactics, and 7) implementation and evaluation.

Special emphasis will be accorded the utilization of the research findings presented for the improvement or establishment of additional prevention education programs both in countries reviewed and elsewhere utilizing marketing.

MP.174 Relationships Between Knowledge About AIDS Risk and Actual Risk Behavior in a Sample of Homosexual Men: Some Implications for Prevention.

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Ninety apparently-healthy homosexual men were administered an objective-format, 33-item test of knowledge about sexual practices high-risk for HIV transmission and a questionnaire eliciting information on sexual activities over the preceding twelve months. All subjects lived in a city where AIDS education brochures are distributed in gay bars.

Correlations were computed between Risk Knowledge Test scores ($\bar{x}$ = 25.6 of 33, range = 9 - 33) and frequency of actual high-risk conduct to examine relationships between risk knowledge and risk behavior. Risk behavior in the sample ranged from very low (0 partners, no occurrence of anal intercourse) to very high (200 partners, 96 occurrences of unprotected receptive anal intercourse). Pearson product-moment correlations revealed that AIDS Knowledge scores were not significantly related to number of different sexual partners ($r = -.02$), frequency of unprotected insertive ($r = +.10$) or receptive ($r = -.15$) anal intercourse, oral intercourse with semen entry ($r = -.06$), meeting partners at "sex clubs" ($r = +.11$), or other risk behaviors. Regression analyses detected no relationships between AIDS risk knowledge and behavior.

Research in other health/behavior areas indicates that information provision alone is often insufficient to change longstanding, immediately-reinforced risk behavior. In addition to informational campaigns, other community-based interventions may be needed to promote risk behavior change. Examples of such approaches, and copies of study measures, will be presented.

MP.175 Clinical and Immunological Features of 100 HIV Antibody Positive Individuals from an Alternate Test Site

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We evaluated 100 HIV antibody positive persons from the only alternate test site in Los Angeles. Sixty-five were asymptomatic (Group 1) and 35 complained of systemic symptoms (Group 2), such as fever (31%), night sweats (61%), fatigue (66%) and weight loss (6%). Twenty-one ambulatory patients with AIDS manifested by a prior episode of Pneumocystis carinii pneumonia within 90 days (Group 3) served as controls. Irrespective of symptomatology, Groups 1 and 2 demonstrated clinical and laboratory evidence of immunodeficiency. Eighty had generalized lymphadenopathy, 16 onychomycosis, 6 oral thrush, and 2 biopsy-proven Kaposi's sarcoma. Despite normal white cell counts, 40 (62%) of Group 1 already had T4 lymphocyte cell counts below 500 cells/mm^3 and 31 (48%) had below 300 cells/mm^3 (mean 468 cells/mm^3). Thirty-one (89%) of Group 2 had less than 500 T4 cells/mm^3 and 16 (46%) had less than 300 cells/mm^3 (mean 324 cells/mm^3). Group 3 had the lowest T4 counts (mean 84 cells/mm^3). Differences between mean T4 cell counts in the three groups were significant ($P<0.001$). In addition, 75% of Group 1, 80% of Group 2, and 100% of Group 3 were anergic to seven intradermal antigens. We believe the high frequency of clinical and laboratory evidence of immunodeficiency in subjects evaluated at the Los Angeles alternate test site justifies the allocation of funding for medical evaluation and follow-up care for other test centers with similar findings.

MP.176 AIDS Educators Perceptions of Barriers to Effective Health Education: Report on a National Survey.

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As part of a project conducted for the American Public Health Association to develop guidelines for effective AIDS education, investigators surveyed a convenience sample of 80 AIDS educators throughout the United States. Twenty-five respondents participated in one to two hour semi-structured interviews, 25 were interviewed on the telephone and 30 responded to a mailed questionnaire. Respondents were educators working on AIDS for public and private agencies

A qualitative analysis of their responses revealed common organizational, educational and political barriers to effective education. Organizational problems included integrating volunteer and paid staff, balancing service delivery and prevention, coordinating public and private efforts, and developing effective coalitions and networks. Educational problems included interpreting scientific information for the public, communicating effectively with diverse populations, inadequate time for planning and difficulties in evaluating the impact of interventions. Larger sociopolitical problems were difficulties in reaching minorities, inadequate resources and public resistance to open discussion about sex and drugs.

Respondents described their assessment of the consequences of these obstacles and how they addressed these consequences. Investigators categorized these descriptions into specific behavioral responses to each obstacle. The report concludes with recommendations for more effective AIDS education.

MP.177 Interactive Simulation as a Tool in the Decision-making Process to Prevent HIV Incidence among Homosexual Men in The Netherlands.

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The current knowledge of the behavioral and physical system of forces which cause the spread of HIV among homosexual men is incomplete and scattered over a wide range of professional journals and reports. At the same time, the discussion on what the effect of certain preventive measures on behavior of the population at risk will be, is in an early stage. The use of a computer stored diffusion model on HIV among homosexual men can be a powerful, although hypothetical, discussion- and decision-aid when considering the dynamic effects of certain preventive measures. Formal models however, are mostly too complicated for an effective and widespread use in this respect. The procedure as proposed here, tries to solve this problem, by an integration of computer simulation with elements of gaming. The result is a so called interactive simulation, in which persons-in-roles interact in a question-and-answer relationship with a formal dynamic model programmed for a computer. The instrument as designed consists of a) a formal computer stored model, in which the existing knowledge on preventive measures and the behavioral and physical side of HIV is defined clearly and b) a computer interaction procedure to perform simulation experiments with preventive measures and c) a discussion procedure for a group of persons with eachother and in interaction with the computer stored model, to explore and evaluate the short- and long term consequences of preventive measures on the spread of HIV among homosexual men.

MP.178 AIDS Prevention, Information and Education for Health; a model for a comprehensive strategy focused on the general public as well as special target groups; practised in the Netherlands since 1983.

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In 1983 the national government, public health authorities and organisations affiliated with groups at risk for AIDS, joined hands and concluded that a communication strategy had to be developed with the object to inform and educate the population about possible HIV infection.

Inside the model for the strategy, two general objectives were determined: (1) to help reduce the spread of infection, (2) to counteract prejudice and misconceptions as well as unjustified anxiety and fear.

It was assumed that a 'step by step' approach had to be adopted: a short term strategy (supplying knowledge = one way communication) and a long term strategy (a process of systematized two way communication between sender and recipient of the message in order to condition attitudes and values).

In practice it meant that first attention was given to groups at risk which were approached by both health information and health education; through the years the prevention activities were extended to larger groups inside the general population and to the general public itself.

Large scale evaluation activities were incorporated in this communication model, with promising results both on the level of knowledge and attitudes (cfv Tielman 1987)(cfv Eyrond 1987); also press coverage in general was informative and could be made part of this process of health promotion.

The dutch approach received positive attention from other european countries and was a starting point for wider activities by The Council of Europe and the European Common Market. The model included active participation of advertising agents and marketing officers.

MP.179 AIDS Information and Prevention Concept in Switzerland

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1. Initial position: All available epidemiological data show that, with respect to frequency of cases of AIDS and HIV infection, Switzerland leads the statistics for European countries. Thus, 26 cases of AIDS infection per 1 million inhabitants were recorded by September 1986.
2. Consequently, the federal health authorities have conducted various informative campaigns in conjunction with the Swiss AIDS Foundation since end 1985. For example, in March 1985 a brochure was distributed to all households. The results of this campaign were evaluated.
3. Since February 1987 the same instances have been running a national campaign stressing the features:
   a) use of the condom for all risk factor sexual contacts.
   b) no sharing of syringes for i.v. use of drugs.
   The results of this campaign will also be evaluated.

The close cooperation between the official body (Federal Ministry of Health) and the private organization (Swiss AIDS Foundation) has been very fruitful to date. The work is explained briefly and the objectives and elements of the campaign and their evaluation presented.

MP.180 AIDS Prevention among Homosexuals in Switzerland

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1. Initial situation: All available epidemiological data show that homosexual and bisexual men still constitute the major group effected. Thus, 109 of 170 (=64 %) cases are accounted for by this group. Epidemiologists estimate that some 15 % are infected today.

2. Objective: Prevention of new infection within this target group by education. All are aware that anal sex constitutes a high infection risk. All are aware that protection is possible in sexual contacts outside a monogamous relationship of at least 6 years' duration by practising Safer Sex (= no unprotected anal practises, no sperm in the mouth).

3. Procedure: The AIDS prevention campaign comprises three features:
- "The Hot Rubber": The Swiss AIDS Foundation operates the "Hot Rubber Company" and markets the condom ("The Condom for the Gay Man") at all meeting points (bars, saunas etc.) and by direct mail. A poster campaign with "poster of the month" feature backs up the publicity.
- The Safer Sex Campaign: With brochures, posters, advertisements and articles the Swiss AIDS Foundation draws attention to Safer Sex on the Swiss scene.
- Discussion groups: Local AIDS Help group in conjunction with homosexual groups stage regional workshops on the subject of sexuality. The Swiss AIDS Foundation operates the national hot line to safer sex.

4. Evaluation: A first cross-section inquiry will be conducted in January 1987. Later, inquiries will be conducted every 6 months which should provide qualitative results.

The concept will be illustrated briefly, with examples, and the first evaluation presented.

MP.181 An Evaluation of Using Ex-addict Outreach workers to Educate Intravenous Drug Users about AIDS Prevention.

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We sent ex-addict outreach workers to randomly assigned areas of Baltimore to teach intravenous drug users (IVDU'S) about the dangers of AIDS. Interviews conducted before and one month after the intervention (85% of followups completed) with IVDU'S in experimental and control neighborhoods measured knowledge of AIDS and the frequency of high risk behavior; we also collected data on the number of experimental subjects who entered drug treatment, obtained an antibody test or sought additional information from an AIDS hotline. The results showed that the outreach approach was feasible and effective in finding IVDU'S who were not in treatment and getting them to listen to a message and accept pamphlets on AIDS. The experimental subjects (n=236) had significantly more knowledge of AIDS at followup than did the controls (n=72), but behavioral changes (e.g., sharing and cleaning needles, use of condoms and obtaining an antibody test) were not significant. We concluded that this was an effective educational approach, but that greater behavior change would require more concrete interventions, e.g., distributing condoms and pocket-size bottles of bleach, making entry into treatment easier and bringing antibody testing to the street corners.

MP.182 Prevalence of Antibody to Human Immunodeficiency Virus (HIV) and Client Characteristics in the Wisconsin Alternate Site Testing and Counseling Program, 1985-86

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In June, 1985 a program providing free and anonymous HIV antibody testing and counseling began at 30 sites other than blood or plasma centers in Wisconsin. As of December, 1986, 2856 clients had been counseled and completed a self administered questionnaire; 2789 HIV antibody tests were performed, of which 245 (9.5%) were repeatedly reactive by enzyme immunoassay (EIA) and 197 (7.7%) positive by Western blot assay (WB). Among gay/bisexual men using IV drugs, 26 (31.7%) of 82 were WB positive compared to 126 (9.9%) of 1272 gay/bisexual men who did not use IV drugs ($p<.001$). Analysis by race demonstrated 23 (40.3%) of 57 black gay males to be WB positive compared to 129 (10.0%) of 1289 nonblack gay males ($p<.001$); none of 31 black heterosexual IV drug users had detectable antibody to HIV. Prevalence of HIV antibody was less than 5% in all groups other than gay/bisexual males. Among gay/bisexual men, 84% reported changes in their lifestyle or sexual practices due to concern about AIDS; 44.8% were not comfortable discussing their lifestyle or sexual practices with their health care provider, but regional differences were noted. In Wisconsin, a state with a relatively low incidence of AIDS, there are subgroups of individuals with a high prevalence of HIV infection, the majority of whom reside in Milwaukee or Dane counties. Intrastate regional analysis of HIV seroprevalence and client characteristics is useful for the development of local educational programs directed toward individuals at increased risk of acquiring HIV infection.

MP.183 Prevention Policy on AIDS among Drug Addicts in Amsterdam

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By Janusry 1st 1987 Aids had been diagnosed among 7 i.v. drug addicts in the Netherlands. In Amsterdam 20-35% of the i.v. drug addicts has been infected by HIV. To prevent or slow down further spread of the virus is therefore of paramount importance.

Apart from drugfree treatment and resocialisation, the Amsterdam helping system consists of (1) contacting addicts in the drugscene, police stations and general hospitals, (2) harm reduction such as medical- and social primary care, methadone prescription (e.g. "methadone by bus project"), needle and syringe exchange and (3) health education.

This approach is essentially non-moralistic. About 70% of the addicts is in touch with this helping system.

Health education and needle and syringe exchange were intensified after Aids became a focal issue. Emphasis is placed on safe-sex and safe-druguse.

Health education is carried out through leaflets, personal contact and condom distribution to addicted prostitutes. Slot machines were also installed to provide addicts with condoms.

Needle and syringe exchange is possible at 13 different locations throughout the city. In 1986 350,000 needles and syringes were exchanged. No increase in needle stick accidents has been reported among the general population.

Preliminary findings show that needle sharing has reduced. Counter effects of the harm-reduction program could not be found: the number of i.v. drug addicts has not increased, while the patient-load of drugfree treatment programmes has doubled over the last 6 years.

MP.184 Knowledge and Attitudes About AIDS Among College Freshmen in Louisiana

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In spring 1986, we mailed an AIDS knowledge and attitude questionnaire to 3231 randomly selected freshmen attending seven universities in Louisiana; 967 responded. Their mean age was 18.5 years; 65% were female. Most (93%) were 1985 high school (HS) graduates, 72% from schools in Louisiana and the remainder from schools in 38 other states. Only 28% responded that AIDS had been discussed in one or more HS classes. The most frequently reported source of information was television (60%).

More than 90% were able to correctly identify major high risk groups for AIDS (homosexual men, intravenous drug users), but 16% and 13% respectively added household members of AIDS patients and blood donors as being at high risk. Although more than 95% correctly identified major routes of transmission (sexual, sharing needles), 14% believed mosquitoes and 6% believed donating blood could transmit the disease. Respondent sex, type of HS, HS location, and discussion of AIDS in a HS class did not significantly affect knowledge score.

Respondents reported that their knowledge of AIDS affected their behavior in the following ways: choice of friends-17%, choice of sexual partners-59%, number of sexual partners-59%, willingness to donate blood-18%.

Our findings indicate that college freshmen in Louisiana are well informed about major risk groups, transmission and prevention of AIDS but that considerable confusion exists concerning blood donation and casual transmission.

MP.185 Knowledge and Attitudes about AIDS in Rhode Islanders
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A random digit dial telephone survey was conducted in December, 1986. Four-hundred questionnaires were completed at a cost of $2,6DO. Fifty-six percent of respondents were women; median age and educational level were 39 years and 12 years respectively.

Overall, general knowledge of AIDS transmission and risk groups was limited. While 86% said AIDS could not be spread by casual contact, 24% thought that sharing the same glass as a person with AIDS was a source of infection. Only 55% of respondents identified drug addicts as a risk group for AIDS and 20% identified hemophiliacs. Forty percent felt that AIDS would not be a problem in their community, and only 38% considered the blood supply safe.

Stratification of responses by age and educational level demonstrated that AIDS knowledge varied directly with educational level and inversely with age. For example, 75% of those with a college education identified drug addicts as a risk group while only 42% of those with less than a high school education did (X^2 test for trend=26.9, p<.05);64% of those under 55 could identify drug addicts as being at risk for AIDS but only 34% of those 55 and over could do so (X^2=27, p<.D5). Those ages 18-24 were more likely than any other age group to have changed their sexual behavior since learning of AIDS (X^2 test for trend=12.2 p<.05).

Such telephone surveys represent a cost-effective method of identifying target groups for educational interventions and if applied periodically, can serve to measure their success.

MP.186 HIV Antibodies in Needles and Syringes Used By Intravenous Drug Users.
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The sharing of needles and syringes by intravenous drug users (IVDU) has been recognised as a critical factor in the transmission of the human immunodeficiency virus (HIV).

A pilot sterile needle and syringe exchange programme was established in an inner city neighbourhood in Sydney, Australia in an attempt to reduce sharing of needles and syringes among IVDU. The contents of exchange syringes were analysed for antibody to HIV by ELISA; the contents of reactive and boarderline syringes were confirmed by Western blot. Of a sample of 300 needles and syringes exchanged, 1% were found to be antibody positive and thus potentially infectious. Analysis of positive and negative control syringes indicated that the proportion of potentially infectious needles found in this study may have underestimated the proportion of infectious injection equipment returned. These finding emphasise the importance of removing used needles and syringes from circulation in addition to supplying sterile equipment. This method of monitoring exchanged needles and syringes is suggested as a means of evaluating measures designed to reduce the transmission of HIV among IVDU. Rapid implementation of sterile needle and syringe exchange programmes is imperative in Western countries to stem the spread of HIV infection.

MP.187 A Survey of Knowledge and Attitudes Among Dentists Concerning AIDS
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AIDS presents many problems for various health care professionals including dentists. This is especially true with the renewed emphasis on infection control in the dental profession.

In order to assess knolwedge of the average practicing dentist concerning AIDS, approximately 1,200 dentists were surveyed concerning AIDS etiology, transmission, epidemiology, oral manifestations, methods of detection, treatment, prevention, and sociological and behavioral attitudes. It was hypothesized that dentists in larger cities with a higher incidence of reported AIDS cases would have a better understanding of AIDS and ARC than dentists in cities with fewer AIDS patients.

The results were analyzed using Pearson Product Moment Coefficient of Correlation (Pearson's r). The results indicated that although there is a correlation between the number of AIDS patients in a city and a better understanding of AIDS by dentists in that city, the increased knowledge did not generalize to all areas surveyed. Other methods of educating dentists concerning AIDS, infection control, and their role as health care professionals concerning patients with infectious diseases are needed.

MP.188 Behavioral Diagnosis for Effective Education of HIV-Seropositive Patients.
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The US Surgeon General and National Academy of Sciences have recently advocated that control of AIDS will require widespread public education. Effective education, in turn, depends on a correct behavioral diagnosis. This paper describes how a behavioral diagnosis is accomplished as a basis for counseling HIV-positive patients. Such counseling should address various co-factors implicated in the progression of AIDS, and measures to stem the spread of the HIV virus.

Previous research reveals the following barriers to making recommended behavior changes: low perceived efficacy of changing sexual behaviors, lack of AIDS knowledge, difficulty in controlling sexual impulses, high belief in biomedicine to cure AIDS, and non-supportive social norms. Additionally, anecdotal experience indicates that several barriers exist to HIV-positive patients seeking regular medical care: denial, social stigmatization, and fears about confidentiality of information.

The paper concludes by describing how the behavioral diagnosis technique can be applied to training health professionals to better care for and educate HIV-positive patients.

MP.189 Prenatal diagnosis of congenital H.I.V. infection
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In order to find a way of distinguishing prenatally between infected fetuses and those who escape infection, we compared, in two cases, fetal blood samples with mother blood samples. Fetal blood was carried out at 24 and 27 weeks of gestation by direct puncture of the umbilical cord under ultrasound guidance, and only before a medical terminaison of the pregnancy.

In these two cases, HIV antibodies were found in fetal blood samples. HIV was isolated from stimulated T lymphocytes and detected by reverse transcriptase activity only in one mother but not in fetuses. Immunological investigations did not demonstrate evident immnunodeficiency : lymphocytes, T4/T8, ratio, platelets were normal. Non specific IgM titers were unelevated and lymphoid tissues did not present lymphocytes depletion.

This preliminary study suggest that prenatal diagnosis of congenital HIV is available using this procedure ; even if many points must be discussed. The theoritical risk of contaminating an uninfected fetus through the fetal blood sampling itself is relevant. The absence of maternal blood contamination in fetal blood has been avoided.

Further studies must etablish if no elevation of IgM and no isolation of HIV from fetal T lymphocytes are sufficient to eliminate HIV congenital infection.

MP.190 AIDS: A Public Health Challenge for States
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The presentation summarizes the findings of a PHS funded document detailing AIDS policy issues for state legislators and key health program officials. Basic policy questions are discussed in twelve major areas including: screening and testing, surveillance, confidentiality, potential discrimination, needs of special populations, education, other modes of intervention, research, medical care, support services, financing and administration. A range of state legislative, program and policy solutions from all fifty states is described, highlighting specific case examples to illustrate how states have developed sometimes different and sometimes parallel solutions to similar AIDS related problems. Basic health policy concepts are also discussed to help states frame their own AIDS programs and policies. Testing, confidentiality and financing issues are emphasized -- the latter focusing on AZT, its reimbursement, allocation, cost effectiveness and implications for developing insurance mechanisms and systems of care for persons with HIV infection. The study recommends that AIDS may be used as a vehicle for developing paradigms for addressing fundamental health policy problems facing the states. These include designing systems for chronic care, financing catastrophic care and care for the uninsured.

MP.191 Disinfection of IV Drug Paraphernalia Using Commonly Available Materials: Hope for Controlling Spread of HIV Among IV Drug Users? SUNITA JAIN*, N. FLYNN*, E. KEDDIE*, J. CARLSON*, S. HARPER*, V. BAILEY**, et al.** *Univ of Calif. Davis, **Aquarian Effort, Sacramento, CA

HIV is spreading rapidly among U.S. IV drug users (IVDU) and will spread widely from them to new populations through heterosexual and vertical transmission (T). We have demonstrated that sharing of paraphernalia (P) continues deapite reasonable knowledge among IVDU of mode of T. Few IVDU regularly practice disinfection of P between users.

We tested the ability of commonly available potential disinfecting agents (DA) to inactivate HIV using a sensitive infectivity assay and questioned IVDU regarding availability of these DA last time they shot up. HIV was not infective after exposure to dilute household bleach or dish detergent, rubbing alcohol, vodka, or wine; beer and cola drink were ineffective. P withstood exposure to each DA at least 50 times without showing significant damage. 70% of IVDU related that one or more of these DA were easily available last time they shot up (bleach 35%, rubbing alcohol 56%, wine 23%, liquid dish detergent 49%). They expressed interest in learning simple techniques for disinfection of P using these commonly available DA. We are developing an instructional program for IVDU in drug treatment programs emphasizing a simple, practical, 2-step disinfection technique in which P are rinsed in any active DA and then in water before being passed to the next user.

In the absence of decriminalization of P and changes in P-sharing habits, disinfection may offer the only hope for slowing the T of HIV among IVDU and, subsequently, to their sexual contacts and offspring. We have identified easily available DA and a simple disinfection technique which is effective in vitro.

MP.192 Follow-up Counseling and Risk Behavior Assessment of HIV Antibody Positive Military recruits

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Military Entrance Processing Stations (MEPS) began screening new recruits in October 1985 by ELISA and Western Blot for HIV antibody (Ab). Positives are not provided interpretation of results or counseling by MEPS. Colorado Department of Health (CDH) regulations require reports of positives with identifiers. Seventeen have been reported to CDH by MEPS (seropositivity rate less than .13%). All reported positives were male (11 white, 3 black and 3 hispanic). The average age for positives (25) is older than negative recruits where the majority are in the 17-19 age group.

By January 1987, CDH completed follow-up on 16 positives and confirmed or provided counseling to 12 (75.0%), (2 were not located, 1 moved out-of-state). Only 1 declined counseling. Of the 12, 11 were retested, with one negative by both ELISA and Western Blot.

Risk behaviors were evaluated for the 11 counseled and retested positives. Although prior to MEPS Ab testing, recruits sign an affidavit denying homosexual/bisexual activity, during the CDH evaluation 10 of 11 positives reported homosexual or bisexual activity as a risk factor. One claimed heterosexual contact with female prostitutes. Four of the individuals reported 2 risk behaviors.

Transmission prevention counseling is essential for positives. Public health follow-up ensures counseling, permits risk assessment and may identify pools of heterosexual HIV infection.

MP.193 Minnesota Counseling and Testing Sites: Analysis of Trends Over Time. RICHARD N. DANILA*, J.M. SHULTZ*, M.T. OSTERHOLM*, K.L. MACDONALD*, K. HENRY**, M. SIMPSON***. *Minnesota Department of Health, **St. Paul-Ramsey Medical Center, ***Hennepin County Medical Center, Minneapolis, MN, USA.

Counseling and testing sites (CTS's) opened in MN in July 1985 to provide HIV antibody testing (with Western blot confirmation) to persons at high risk for acquiring HIV infection. Data obtained during the first 12 months of operation (4,906 client visits for 4,598 clients) were analyzed to assess trends over time. The overall seroprevalence rate for all visits was 10.8%. Among males, the highest seroprevalence rates were in homosexual men (422/2440 [17.3%]). This rate did not change over time; however, the proportion of clients who were homosexual men significantly decreased over time when compared to the entire group ($p<0.01$). Thus, the overall monthly seroprevalence rates declined significantly ($p<0.01$). The number of repeat visits increased significantly ($p<0.01$); however, this did not account for the observed decline in seroprevalence, because rates of seropositivity were similar for first-time and repeat visits (497/4,598 [10.8%] vs. 30/306 [9.8%]). During this time, a significant increase in the number of women clients being tested was noted ($p<0.01$). Because the seroprevalence rate for female clients was very low (5/638 [0.8%]), the increasing proportion of female clients may have also contributed to the overall decline in the observed seroprevalence rate. Increases over time were noted in the number of heterosexual clients with sexual exposure to a high-risk partner, the number of clients reporting an HIV-antibody positive sex partner, and the number of clients with an unspecified risk or no risk. These changing client demographics may have public health implications for designing outreach programs aimed at counseling and testing persons at highest risk of exposure to HIV.

MP.194 Standardized Scales and Documentation of AIDS-HIV Knowledge and Prevention for Health Care Professionals and the Public

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The epidemic of AIDS and Human Immunodeficiency Virus (HIV) infections presents new problems in educating health care professionals and the public. These problems include: (1) rapid accumulation of biomedical information which may be relevant to clinical practice; (2) new concepts in pathobiology specific to HIV infections; (3) phobic blocks associated with groups at higher risk which may preclude unbiased assimilation of information on HIV; and (4) the character of an expanding epidemic which increasingly affects many aspects of society. Due to these issues, traditional means of education are inadequate to deal with the necessary dissemination of information on HIV. In addition, a lack of standardization of AIDS information may enhance misconceptions, facilitate false information, and markedly detract from optimal clinical care of patient with AIDS or ARC. Misconceptions and false information on AIDS will only spread the epidemic even more. AVERI, AIDS Virus Education and Research Institute, was founded in 1984 to deal with these issues. AVERI provides educational programs about AIDS for various sectors of the public and continuing education about AIDS and HIV for health care professionals. Also, AVERI, in conjunction with its Medical Advisory Board, has devised three standardized scales to document assimilation of AIDS information. No one (lay or physician) should be providing counseling or educating others about AIDS without a passing score on one of the scales. The first is "BAPS," Basic AIDS Prevention Scale, for the lay public. Second is "AAPS," Advanced AIDS Prevention Scale, for health care professionals and health care employees. For health care professionals treating AIDS and ARC patients, there is "AAPTS," Advanced AIDS Prevention and Treatment Scale. In the opinion of the AVERI Medical Advisory Board, 85% of all hospital personnel should achieve a passing score on "BAPS" and all hospital and pre-hospital health care professionals should be able to pass "AATS" if not "AAPTS." Widespread use of these 3 test scales, along with quality AIDS-HIV education will decrease the spread of the epidemic, decrease AIDS phobias, and optimize care of the AIDS patient.

MP.195 Psychological Reactions of Individuals at Risk for AIDS Participating in an Experimental Drug Trial

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Administration of anti-viral agents has been proposed as a means of preventing the development of AIDS in asymptomatic individuals infected with HIV. However, since these individuals typically feel physically well and, in addition, may be psychologically distressed because of their risk status, there is concern about their willingness to adhere to an experimental drug trial. The present study addressed this question by studying 26 homosexual/bisexual males enrolled in a randomized double-blind trial of ribavirin. Subjects were without manifestations of AIDS or ARC, but were HIV antibody and viral positive. Standardized self-report measures of psychological distress (Brief Symptom Inventory) and perceptions of treatment were administered during the first 2 weeks of the drug study and, again, 8 weeks later near the end of treatment. Results indicated that mean levels of distress at the initial assessment were 2 to 3 standard deviations above norms for the general population but were similar to norms for psychiatric outpatients and for other populations at risk for AIDS. Analysis of variance showed that mean levels of distress remained unchanged between the initial and follow-up assessments. In addition, T-test comparisons demonstrated that the intensity of distress at both baseline and follow-up was unrelated to patients' beliefs about whether they were receiving active drug or placebo. None of the 26 patients refused to continue participation in the drug trial during the period of study. These findings suggest that, while asymptomatic seropositive individuals may remain psychologically distressed, they are likely to continue to adhere to placebo-controlled trials of anti-HIV drugs.

MP.196 Physician Attitudes and Stigma Associated with an AIDS Diagnosis

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A randomly-selected sample of 163 physicians practicing in three cities (Columbus, OH, Memphis, TN, and Phoenix, AZ) were subjects in a study assessing attitudes towards AIDS. These cities are the largest in states which rank near the midpoint for AIDS prevalence. Each physician/subject read a 500-word vignette describing a male patient; vignettes were identical except that the patient's illness was identified as either AIDS or leukemia and the patient was identified as either homosexual or heterosexual. Subjects completed objective measures assessing attitudes toward the patient after reading a randomly-assigned vignette.

Multivariate ANOVAs showed that AIDS patients were considered more responsible for and deserving of their illness, dangerous, deserving quarantine, and less deserving of sympathy (all $p < .05$ to $p < .0001$). Physicians reported markedly less willingness to interact with an AIDS patient than an identically-described leukemia patient in such contexts as conversation ($p < .01$), working in the same office, living in the same apartment building, attending a party, or continuing a past friendship (all $p < .0001$).

As HIV infection prevalence increases outside the nation's largest cities, physicians in all practice specialities will see many more HIV patients. Health-care providers may share some of the same attitude prejudices as the general community. There is a need to develop better psychological/education programs for health-care providers especially in areas where AIDS prevalence will soon increase.

MP.197 An AIDS Training Program for Mental Health Professionals

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An AIDS mental health training program was developed in 1986 through a collaborative effort of New York City Department of Mental Health, the Memorial Sloan-Kettering Cancer Center Department of Social Work and the Gay Men's Health Crisis. To date, over one thousand professionals from voluntary and municipal hospitals, community mental health centers, social service agencies and chemical dependency units have participated.

An initial needs assessment revealed that generic information about the medical and psychosocial aspects of AIDS was not sufficient. Substantive areas identified for training included: fears of contagion; countertransference issues relating to homophobia, aversion to treating drug addicts, feelings of hopelessness and helplessness, and emotional overwhelm or bereavement; work with the medically and terminally ill; coping with the enormity and intensity of patient needs; maintaining updated medical information. Five additional substantive areas were requested; drug addiction, minority culture issues, neuropsychiatric issues, family and relationship therapies.

Pre-intervention evaluation revealed that participants had high levels of knowledge of AIDS which were not significantly increased through participation in the program. Positive change was observed at the end of the training in the following areas: 73% reported more optimism in helping PWAs cope with their illness; 75% reported greater empathy for PWAs; over 80% indicated they were more confident of their AIDS knowledge; over 80% were more aware of the psychological and medical needs, and over 60% indicated increased confidence in their ability to deal with value and lifestyle differences with patients.

MP.198 Control of Hypersexuality in HIV Carrier

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A homosexual man with AIDS Related Complex sought psychiatric treatment because of anxiety associated with hypersexuality. He reported that he had unprotected sex with as many as 40 anonymous partners weekly in bath houses; he said he recognized the health hazard to himself and others posed by his behavior but could not control his sexual drive. He gave written consent to weekly intramuscular injections of medroxyprogesterone acetate, which rapidly and profoundly lowered his testosterone level and reduced his sexual urges. He also received supportive psychotherapy and antidepressant medication, with marked mood improvement. Side-effects of the anti-androgen included mild hypertension that required antihypertensive medication. This case report suggests that a subset of HIV carriers who remain sexually promiscuous may have an atypical paraphilia that is responsive to combined psychotherapeutic and pharmacologic measures.

MP.199 Support Groups for HIV Positive Women Including Those With HIV Positive Infants.

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Epidemiological studies suggest that at present the seroprevalence rate among sexually active heterosexual women in the San Francisco Bay Area is between 0.5% and 5%. A need was felt in 1985 to create support groups for HIV positive women. Initially these efforts were unsuccessful. In September, 1986 the Women's AIDS Network tried again to establish support groups for HIV positive women. As of January, 1987 one group for HIV positive women has been established in San Francisco, and several other groups are forming including one for seropositive transexuals.

This poster is planned to share our experiences:

A. Establishing groups for HIV positive women: planning effective outreach strategies and addressing the importance of anonymity and confidentially.
B. Group structure and client issues found to be effective.
C. Addressing different needs for different clients i.e., women who have by vertical transmission infected their children as opposed to single women with multiple partners, or IV drug users.

The psychosocial needs for HIV positive women are complex and often different from homosexual men. Support groups can help provide problem-solving, educational, and emotional support, and at the very least "a safe place" to share experiences in order to reduce feelings of isolation.

MP.200 Psychiatric Illness in HIV-Infected Men & Controls

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Psychiatric complications in hospitalized patients with acquired immune deficiency syndrome (AIDS) and AIDS-related complex (ARC) are widely reported, but little is known of the lifetime psychiatric history of ambulatory men with AIDS, ARC, or of asymptomatic men infected with HIV (human immunodeficiency virus). Lifetime prevalence and current psychiatric disorder in men infected with HIV, or at risk for infection were examined using the Diagnostic Interview Schedule (DIS, Version III-A), Profile of Mood States (POMS), and Symptom Checklist-90 (SCL-90). We examined four groups of homosexual men and a comparison group of heterosexual men equated for age and socioeconomic status. The groups were (1) AIDS (N=15); (2) ARC (N=13); (3) Other HIV seropositive (N=16); (4) HIV seronegative (N=11); and (5) seronegative heterosexual (N=22). Results: Among all homosexual men (Groups 1-4) lifetime prevalence of any DIS psychiatric disorder was 80.2%; major depression was 30.4%; alcohol abuse/dependence 32.1%; other substance abuse 39.3%; and anxiety disorder (excluding phobias) 39.3%. There was no significant difference between groups of homosexual men in prevalence of major syndromes. Over 30.3% of men in Groups 1-4 experienced the onset of a DIS-disorder within the previous six months. Group 5 subjects had markedly lower proportions of major depression (10 %) and anxiety disorder (0%). Conclusion: Because lifetime and recent prevalence of psychiatric disorder among ambulatory men infected or at risk for infection with HIV is elevated, longitudinal assessment and early psychiatric intervention may improve patient care.

MP.201 Behavior by Intravenous Drug Users that Can Transmit HIV.

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In New York, intravenous drug users (IVDU) are the main source of HIV transmission to other IVDU and to heterosexual partner and in utero transmission AIDS cases. 195 Manhattan methadone patients were interviewed in 1986 about drug injection, sexual behaviors and child-bearing plans. They had mean frequencies of 22 drug injections per month, of which 4.7 were in shooting galleries; they knowingly let others use their used syringes a mean of 6.6 times per month. 125 male subjects each had mean total sexual frequency of 6 times per month with a mean of 1.8 female partners. On average, each man had .6 regular sex partners who were not IVDU. 61 female subjects each had mean total sexual frequency of 11 times per month with a mean of 2.7 male partners. On average, each woman had .6 regular sex partners who were not IVDU. 59/153 (39%) subjects intend to have further children. 49% of 165 subjects for whom Abbott ELISA and Western blot HIV antibody test results were available were seropositive.

Subjects who had been in methadone treatment for more than 24 months had greatly and significantly lower frequencies of drug-related transmission behavior than those in treatment for lesser periods, although they did not differ significantly in sexual behaviors that can transmit HIV. Drug injection frequencies were 53/month as compared to 5 ($p<.0001$); injection in shooting galleries 12/mo. as compared to .84 ($p<.007$); and the frequency of knowingly letting others use works they had already used was 17/mo. as compared to .76 ($p<.0005$). 39% of 28 women in treatment more than 24 months intended to bear future children, as compared to 69% of 16 women in treatment two years or less ($p<.06$).

IVDU frequently behave in ways that can transmit HIV to other persons. Methadone treatment appears to reduce such drug injection behaviors. Since methadone patients engage in considerable potentially risky sexual behavior, AIDS education in such treatment programs should include counseling about heterosexual and in utero transmission.

MP.202 Psychosomatic Distress and Depressive Symptoms Among HTLV III/LAV Seropositive, Seronegative, and Untested Homosexual Men

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Knowledge of HTLV III/LAV infection is sometimes advocated as a means to encourage behavior change. However, such knowledge can also have a negative impact on psychosocial functioning. The current study examined levels of common somatic complaints and depressive symptomatology in a sample of 150 gay men, none of whom had been diagnosed by a physician with AIDS or ARC. The sample was divided into three groups: those who reported positive HTLV III/LAV blood testing results, those who had been found to be negative, and those who had not had a blood test and did not know their HTLV III/LAV infection status. Men indicated the presence or absence of 15 common somatic complaints, 10 were consistent with early ARC or AIDS symptoms and 5 contraindicated an ARC or AIDS diagnosis. Men also completed the CES-Depression Scale. Results indicated that the men who tested positive reported significantly more somatic complaints, more AIDS-related complaints and greater levels of depression than either men who tested negative or who had not been tested. They also showed a trend to report more AIDS-unrelated somatic complaints. Men who tested negative and those who had not been tested did not differ significantly from each other on levels of somatic complaints or depression. Results suggest that knowledge of a positive HTLV III/LAV result may have negative consequences for psychosocial functioning, but a negative result does not lead to less distress than not knowing.

MP.203 Patterns of Heterosexual Contacts Among Intravenous Drug Abusers; Implications For the Heterosexual Transmission of the Human Immunodeficiency Virus

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There is a scarcity of knowledge about the sexual behavior patterns of the intravenous drug abuser (IVDA), despite the potential role of this group in the heterosexual transmission of AIDS. Using a representative sample of 100 clients of the Addiction Research and Treatment (ARTC), who consented to be anonymously interviewed, this study investigated sexual behavior patterns in this sample of intravenous drug abusing clients.

Chi square analyses indicated that at the .001 level of significance, IVDA males were more likely than IVDA females to report heterosexual contacts which were non-IVDAs. Further, among those most likely to have been exposed to AIDS, either by reported needle sharing and/or sexual contact with other intravenous drug abusers, gender was associated with the number of non-IVDA heterosexual contacts at the .001 level of significance. These findings were supportive of other studies which have suggested the potential for an epidemic spread of the AIDS virus among non-IVDA females with IVDA partners.

MP.204 Use of the "Needle Guard" in the Prevention of Needlestick Injuries.

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The "Needle Guard" system was evaluated during a 21 month period during which 454,000 venepunctures were performed. It was shown that "Needle Guard" users incurred a needlestick once in every 23,546 venepunctures, whereas, non-users of the "Needle Guard" incurred an accident once in every 4,929 venepunctures ($p<0.001$).

This 79.9 percent reduction in needlestick accidents attributable to the "Needle Guard" calls for a review of the non-recapping guidelines issued by the Centers for Disease Control.

MP.205 The AIDS Epidemic: A Projection of Its Impact on Hospitals, 1986-1991

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The AIDS epidemic in the United States will have a dramatic impact on the health care delivery system, especially hospital facilities. By 1991, 12,831 hospital beds in the U.S. will be occupied by AIDS patients, more than by lung cancer patients or automobile accident victims. In San Francisco, one of every 10 hospital beds and 19 cents of every dollar spent on inpatient and outpatient therapy will go to treatment of AIDS. In New York, bed need for AIDS will nearly triple from 645 beds in 1986 to 1,753 beds by 1991. In the rest of the country outside these cities, the level of hospital utilization by 1991 (1.14% of beds and 3.2% of treatment costs) will be close to what is being experienced in New York City today. The impact of AIDS on hospital facilities goes beyond these numbers. AIDS patients require added infection control precautions, nursing care, supplies, and complex case management services. Perhaps the most difficult challenge is to face the task of treating young patients with a ravaging disease without the ability to offer a cure.

Dr. Green served as consultant to the Institute of Medicine, National Academy of Science's Task Force on a National Strategy for AIDS. This paper was prepared as background for the Institute's report, Confronting AIDS - Directions for Public Policy, Health Care, and Research.

MP.206 Utilization of Nurse Practitioners in the SFGH AIDS Clinic.

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The rapid expansion of the outpatient AIDS clinic at San Francisco General Hospital required an increase in primary health care providers. Nurse Practitioners were added to augment the medical staff, and have an expanded role within the clinic. During most clinic sessions both physicians and nurse practitioners see patients. Nurse practitioners carry their own caseload, guided by protocols and working in consultation with clinic physicians. Two clinics are run solely by the nurse practitioners. One is for studying and monitoring investigational drug trials. The second is a unique AIDS screening clinic, developed in response to a growing concern by an increasing number of high risk individuals, who have no prior diagnosis of ARC or AIDS. After formal clinic sessions, the nurse practitioners remain available for medical backup, to provide coverage for assessment and triage of emergencies and for telephone consultation. This is a presentation of a descriptive paper addressing the expanded nurse practitioner role within the AIDS clinic, the advanced knowledge needed, and how guidelines and protocols for nurse practitioner practice were developed to meet the needs of the clinic.

MP.207 Oral manifestations of HIV infection: Suggested EEC classification and prevalences in a Danish sample.

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On 16-17 September 1986 the EEC convened a meeting in Copenhagen on oral problems related the HIV infection. During the meeting a tentative classification of 31 oral lesions in patients infected with HIV was agreed upon. The classification divides the lesions into fungal, bacterial & viral infections, neoplasms, and lesions of unknown etiology. Previously infections with Candida albicans have been called oral candidiasis or oral thrush. However, there is a need for dividing candidiasis into pseudomembranous, erythematous and hyperplastic types. In the past a number of the erythematous type of candidiasis have been overlooked. The classification has been applied to 130 HIV infected patients at the University Hospital of Copenhagen. Of these patients 38 had AIDS, 16 ARC and 76 were just seropositive. Sixty-eight percent had one or more oral lesions considered associated with the HIV infection. Candidiasis was found in 41%, hairy leukoplakia in 37% and necrotizing gingivitis in 10%.

MP.208 Multiple Funding Sources for Comprehensive AIDS Public Health Services

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The population most seriously affected by AIDS in New Jersey consists of IV drug addicts, their sexual partners and children. Because this population has limited financial resources and political/community support, and because federal funding for public health services is limited, the NJSDH has had to take the lead in providing services. The Department's role has been to provide seed money to develop and implement programs while identifying other long-term funding sources to support ongoing service delivery. A key element in the Department's strategy has been an increase in drug abuse prevention and treatment.

The Department has sought to substitute a continuum of alternative care services for lengthy stays in acute care facilities. Funding for the alternative care has been sought from a variety of sources--state, federal, private (Robert Wood Johnson) foundation, and Medicaid. Effective use of the resulting mix of funds requires creative administration. Federal and state funds support specific projects and personnel in unit projects; those from the private foundation support in-hospital case management, post-hospitalization services, and education. Supplemental funds from the state support direct services not reimbursable elsewhere. The Medicaid waiver supports home/community care for individuals as an alternative to hospitalization. A matrix will correlate the funding mix with the continuum of services planned by the state.

MP.209 Influence of disease and casemix severity on the hospital costs of caring for AIDS patients. by Mary M. Fanning, T. Harmon, F.A. Shepherd, H. Vellend, S. Minnick, Dept. of Medicine, University of Toronto and Travenol Management Services, Deerfield, Illinois.

The estimated total cost of medical care for a patient with AIDS varies considerably among several published studies and may reflect differences in efficiency of care, disease severity of the hospital case mix as well as accounting practices. Seventy-four percent of all AIDS admissions to Toronto General Hospital between January 1983 and December 1985 were classified into five diagnostic categories: simple Kaposi's sarcoma (S-KS), complex KS (C-KS), simple Pneumocystis carinii pneumonia (S-PCP), complex PCP (C-PCP), and Central Nervous System disorders (CNS). The average cost per admission was calculated by methodology used by Travenol Management Services. Costs were lowest for S-PCP ($Canadian 11,822) and S-KS ($12,020) and increased for the other admission diagnoses: CNS ($15,716), C-KS ($18,045) and C-PCP ($26,395). Daily hospitalization costs also varied among the groups: S-KS and C-KS - $560/d, S-PCP $630/d, CNS $700/d and C-PCP $906/d and all were greater than the average hospitalization costs for non-AIDS patients. Incremental costs of caring for a patient with AIDS compared to a non-AIDS patient were at least 31% greater and led to a net loss to the hospital. Admission diagnoses over the course of illness varied considerably among patients categorized as KS or PCP at initial diagnosis. Case mix changed over the observation period with increased severity of disease and costs. A forecasting formula was derived and demonstrated the influence of observed and projected changes in case mix severity on total yearly hospital costs for AIDS patients. Strategies for cost containment will be discussed.

MP.210 AIDS/ARC Patients in Residential Drug Treatment Therapeutic Communities: A Special Program

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In New Jersey, where IV addicts comprise the majority of AIDS cases, many patients continue to use drugs after diagnosis, have no stable living arrangements, and are non-compliant with medical regimen. They continue to transmit HIV by needle-sharing, sexual contact and perinatally. This paper describes an effort by the NJSDH to address these issues by providing funding for 30 beds in 5 residential drug treatment therapeutic communities for AIDS/ARC patients.

Programs were contracted to provide 1) daily RN contact, 2) weekly physician contact, 3) 5 hours MA level therapy weekly, 4) nutritional support, 5) prescribed medications and supplies, and 6) transportation and liaison with AIDS treatment facilities. Patients were referred by hospitals and other agencies to NJSDH, where records were screened and patients placed. To be eligible, patients must be ambulatory and capable of self-care, alert and oriented, and willing to accept a structured residential environment. By January 1, 1987, out of 60 referrals, 30 patients had been successfully placed. Problems have included cooperation of referral sources, referral of nursing home level patients, patient acceptance of environment, program willingness to modify concept and practice to accommodate social, psychological, and pharmacological needs of AIDS patients.

MP.211 Chronic Care for AIDS Patients: The Health And Hospitals Corporation Model for Long Term Care

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The NYC Health and Hospitals Corporation, as the largest provider of hospital care to AIDS patients in the country, cares for the many patients who remain hospitalized after medical clearance but for whom post acute care placements are not available. About half of this population is homeless, the remainder are certified for some form of long term care Skilled Nursing Facility (SNF) or Health Related Facility (HRF) care.

HHC is currently providing long term care to a number of such patients in "chronic care" beds at two of its facilities. Key elements of this service modality are explored: referral and assessment, intensity of medical care, relationship with acute care facilities and cost/revenue issues.

MP.212 The Adequacy of Hospital Reimbursement for AIDS Patients

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Hospitals are having to balance the competing forces of cost containment efforts by third party payors with increasing numbers of AIDS patients who require particularly costly treatment. Reimbursement to hospitals for AIDS patient care has important financial consequences for hospitals and patients, and could affect quality and access.

An analysis of 169 AIDS admissions between 1982 and 1986 at two hospitals in Washington, DC explored the proportion of hospital costs met by various payors and the efficacy of DRG reimbursement for AIDS patient care.

Preliminary results suggest that commercial insurers (64 cases) paid approximately 24% above estimated cost, while Blue Cross/Blue Shield (40 cases) paid at about cost. The percentage of cost paid by Medicaid (15 cases) differed substantially between admissions, but surprisingly the vast majority fell between 5% below and twice the estimated cost. Those who are without insurance (17 cases) were able to pay only 5% of the cost of treatment, suggesting that hospitals have a strong incentive not to admit these patients.

DRGs in which AIDS patients are commonly placed could result in the under-compensation of hospitals (eg. DRG 398) or over-compensation (eg. DRG 79). This suggests that if third party payors adopt DRG based reimbursement strategies in the future, or if AIDS patients become Medicare eligible, DRGs frequently used for AIDS patients will need to be adjusted, or new DRGs specifically designed for AIDS patients be created.

MP.213 Foster Care Needs of Children with HIV Infection

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Children with perinatally acquired HIV infection are members of multiproblem families. Of 50 families with 57 children, 17.5D (42%) of the families were known to the family protective agency (New Jersey Division of Youth & Family Services [DYFS] prior to the diagnosis of HIV infection. The families were referred for neglect (3/17), abuse (2/17), and foster care placement (12/17). In addition, 3/50 families were referred after diagnosis for neglect (1/3) and placement support services (2/3). 21/57 children are in foster care because of the following: death of a parent (4/21), illness of a parent (2/21), and inability or unwillingness of the parent to care for the child (15/21). Identifying a foster home or facility willing to care for a child with AIDS is difficult. Placement within the extended family occurred for 15/21 children and 6/21 children were placed in DYFS approved foster homes. All placements were maintained although extensive support to the foster family was required once the child was diagnosed. Extended family members require education about the disease as well as ongoing social and financial support if the placement is to be successful. Human services agencies must be willing to care for these children. Health care providers must be available to inform prospective foster parents about the disease and assist foster parents deal with the health care system.

MP.214 Prevalence of Human Immunodeficiency Virus (HIV) Antibodies in Prostitutes and their Clients in Addis Ababa, Ethiopia.

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To determine the prevalence of antibody reactivity against HIV infection we studied 230 subjects, 60 prostitutes and 70 male clients who were seen at three local clinics because of venereal disease complaints, and 100 control subjects from the out-patient department of ALERT. Out of the 230 study subjects 4 female prostitutes, 2 male clients and 1 from the control subjects were found to be positive by the Organon ELISA test. However, when the confirmatory test was done by Western Blot assay only the 4 prostitutes and 1 male client were seropositive showing reactivity to HIV polypeptide antigens of p^{24}, p^{34}, gp^{41}, p^{55}, p^{64}, gp^{120} in molecular weight. These sera were retested and confirmed positive by the State Bacteriological Laboratory in Sweden. This limited seroepidemiological study has determined seropositive individuals without clinical disease within the Addis Ababa geographical region. The low number of seropositive individuals within the population tested suggests a more recent establishment of HIV infection within this high risk behaviour group than in equivalent studies of prostitutes and sexually active individuals reported from other geographical regions of Africa.

MP.215 The Rising Demand for Hospital Beds by AIDS Patients and the Fiscal Implications for Globally Budgeted Hospitals

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To evaluate the growing demand for hospital beds by AIDS patients, we analyzed the hospital utilization rates of AIDS patients followed at the Royal Victoria Hospital (RVH) from 1981-1986. As of December 31 1986, 79 AIDS patients have been treated and 65 (82%) have been hospitalized resulting in 138 admissions ($\bar{x}$ = 2.1 adm./pts.). While the number of AIDS patients diagnosed each year has incressed 14.5 times, the annual admission and inpatient occupancy rates have increased approximately 29 times. During the same period, the total number of available medical beds has remained constant.

YEAR	TOTAL	1981	1982	1983	1984	1985	1986	CHANGE=(1986-81)/81
New Cases	79	2	3	4	14	25	31	14.5
Admissions	138	2	4	5	21	45	61	29.5
Hospital Days	3512	61	124	242	274	962	1849	29.3
Mean Stay	29.1	30.5	31.0	48.4	13.1	21.4	30.3	

Our data indicate that the growth in demand for hospital beds by AIDS patients has exceeded the rise in the number of cases treated at the RVH. In 1986, 2.8% of all medical beds were occupied by AIDS patients. Should this trend continue, AIDS patients will significantly increase the competition for scarce hospital beds. This increased demand for hospital resources will be further compounded if AIDS patients require more services in hospital than the average non-AIDS patient. Fixed global hospital budgeting, as practiced in Quebec, will not be able to respond to this change in csse-mix and demand for services unless precise costing of the services used by AIDS patients is undertaken and health care planners respond appropriately.

MP.216 Ampligen Therapy for HIV Related Immunodeficiency.

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Ampligen, a mismatched dsRNA which inhibits HIV replication in vitro,was given to eleven HIV infected patients with ARC or AIDS to study the anti-viral and immunomodulating effects of this drug. There was no drug toxicity or side effects seen. Seven ARC patients received 200mg twice weekly for 12-16 weeks and 5 were then placed on 100mg twice weekly as a maintenance dose. Four AIDS patients received 250mg twice weekly and this dose was maintained in 2 and doubled in 1 based on clinical response measured at 8 weeks. All patients were HIV culture positive and anergic by multiple skin tests at the start of the study. All patients demonstrated reversal of skin test anergy within 8 weeks. Lymphadenopathy resolved in 3/5 patients. In one patient both hepatosplenomegally and parotid enlargement resolved with Ampligen. Chronic oral candidiasis resolved in another patient. One patient developed PCP for the second time and died after 7 weeks of therapy. No other AIDS related events were noted. In 9/11 patients there were changes in viral parameters: 1/9 became negative by lymphocyte co-culture,P24 antigen concentration decreased in 2/5. In 7/8 mRNA levels and in 7/10 HIV polymerase concentrations decreased. T4 levels improved in 3 and stabilized in 8 patients. After 6 weeks of maintenance therapy, patients remain asymptomatic with intact DTH responses and no change in T4 levels or T4/T8 ratios. The clinical improvement noted in these patients paralleled the apparent viral suppression. These promising results and the absence of drug related toxicity,support the use of Ampligen in additional trials in HIV infected patients.

MP.217 Intravitreal Ganciclovir (BW B759U) in the Management of Cytomegalovirus Retinitis

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Eight patients with unilateral or bilateral CMV retinitis associated with the acquired immune deficiency syndrome were admitted to a protocol designed to evaluate the efficacy of Ganciclovir (BW B759U) administered by the intraocular route. All patients had been treated previously with intravenous Ganciclovir; however, thrombocytopenia and/or leukopenia had necessitated the interruption of intravenous therapy.

In each case, two hundred micrograms of BW B759U dissolved in 0.1 ml Balanced Salt Solution were injected into mid-vitreous through the pars plana under ophthalmoscopic visualization, with retrobulbar anesthesia. Careful attention was directed to minimizing the likelihood of introducing bacteria into the vitreous, to the maintenance of blood flow through the retinal vasculature, and to rapid normalization of intraocular pressure after the injection.

Suppression of the retinitis was observed in seven of the ten treated eyes. Two eyes did not improve. One eye developed a retinal detachment as a result of the procedure. Of ten treated eyes, eight required reinjection within two to twenty days to maintain suppression of the retinitis. The optimum schedule for reinjection is currently unknown.

The intravitreal route of administration of Ganciclovir is well-tolerated by the eye and is associated with reasonable success in suppressing CMV retinitis. It offers an alternative for maintaining vision in patients unable to tolerate intravenous Ganciclovir.

MP.218 Observations on Clinical and Immunologic Parameters in AIDS/ARC Patients Treated with IMREG®-1

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Patients with AIDS or symptomatic ARC were enrolled in three studies of 16 patients each. Each group received IMREG®-1, an immunoregulator derived from healthy human leukocytes, as follows: Group A: Once every four weeks, subcutaneously; Group B: Once every two weeks, subcutaneously; Group C: Once every two weeks, intradermally. The purpose of these studies was to determine if IMREG®-1 could be safely administered in multiple doses, and to follow changes in immune parameters and clinical indicia of these parameters in these patients during treatment.

Delayed hypersensitivity to tetanus toxoid returned or increased in 47, 57 and 75% of patients, while the average number of $T4^+$ cells increased or were unchanged in 31, 44 and 81% of patients in groups A, B and C respectively. $T4^+$ (helper) cells increased by 42%, 36% and 56% in the 5, 7 and 12 individuals of each group that demonstrated increases in $T4^+$ cell number.

During the treatment period there was no observed toxicity attributed to the drug. No new opportunistic infections or deaths were observed, while patients were on protocol. Hematologic parameters appeared to stabilize. Resistant candida infections responded to treatment. Some patients gained weight, while in others there was no weight loss. We observed a decrease in serum uric acid and immunoglobulin levels which may reflect decreased white blood cell destruction and modification of excessive non-specific B cell function. A Phase III randomized placebo control clinical trial in symptomatic ARC and recent onset Kaposi's Sarcoma patients is in progress and will enroll 150 patients. Each patient will be followed for six months of treatment or until an endpoint is reached.

MP.219 Evaluation of Antitrypanosomal and other Antiparasitic Drugs in the Therapy of Experimental Pneumocystis carinii Pneumonia (PCP)

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New drugs are needed for the treatment of PCP in AIDS. We have compared antiprotozoal agents with other antiparasitic drugs in the treatment of experimental PCP. Rats were given corticosteroids for 8 weeks to induce PCP. The drugs were administered during weeks 5-8, and therapeutic efficacy was judged by examining lungs for PC using a semiquantitative histologic scoring system in formalin fixed sections and counting organisms in lung homogenates. Cationic antitrypanosomal agents were the most active compounds: diminazene, imidocarb, amicarbalide, quinapyramine, and isometamidium had efficacy $\geq$ that of pentamidine, the standard drug; guanylhydrazone and ethidium bromide also showed some activity. Efficacy and toxicity of these drugs were related to dose and route and duration of administration. With successful treatment, PCP score and counts fell from 4+ (heavy) and 10^9/lung to 0-1+ (neg-light) and 10^5-10^6/lung. The following drugs showed little or no activity against PCP: quinine, quinidine, quinacrine, pentostam, chlorpromazine, spiramycin, pentostam, and astiban.

The data suggest that drugs used in the treatment of a veterinary African trypanosomiasis are highly active in the therapy of experimental PCP. Since efficacy in the rat model has usually been predictive of success in humans, these compounds represent a new therapeutic approach to PCP with important potential clinical application.

MP.220 **Effects of DHPG on Severe Cytomegalovirus Infection in AIDS**

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Cytomegalovirus (CMV) infection counts for much morbidity and mortality in AIDS. DHPG, a new acyclic nucleoside analogue of guanine has good antiviral effects against CMV in-vitro. We studied efficacy and safety of DHPG, 2.5 or 5.0 mg/kg body weight i.v. during 14 days, in clinical CMV infection in AIDS patients, CDC classification system IV-C_1 or IV-D. Diagnosis of CMV infection was made on the combination of virological, histological and clinical grounds. A DHPG course was given 20 times in 18 patients for: retinitis (11 cases), pneumonia (5), colitis (3) and spinal cord infection (1): in 3 additional patients diagnosis of CMV pneumonia could not be confirmed virologically; these cases were included for safety analysis only. **Virological results:** CMV positive urine and throat cultures became negative in 13 out of 15 patients within 14 days of treatment, and again positive after cessation in 5 out of 7 evaluable patients, mostly within 3 weeks. **Clinical results:** the spinal cord infection didn't improve, colitis responded well in 2 out of 3, pneumonia in 2 out of 5 and retinitis in 7 out of 11 cases. Retinitis relapsed within 4 weeks after cessation of therapy, so maintenance therapy, 2 times a week 5.0 mg/kg i.v. was instituted with good effect. In 3 patients DHPG was given intravitreally, 0.4 mg per 14 days in order to avoid frequent hospital visits. Results are promising and a pilot study is under way. Thrombocytopenia was seen 3 times (requiring drug withdrawal in 1 case), moderate leucopenia in most cases, reversible after drug cessation. We conclude that DHPG is a relatively safe and effective drug in CMV infection in AIDS patients, especially in colitis and retinitis. However, relapse prophylaxis is needed and platelet and white cells counts should be monitored.

MP.221 Randomized Prospective Trial of Ganciclovir Maintenance Therapy for Cytomegalovrius (CMV) Retinitis

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We report the first randomized prospective comparative study of long-term maintenance ganciclovir therapy for CMV retinitis in patients with AIDS. Eleven CMV retinitis patients who received a ten day course of ganciclovir induction therapy were randomized to receive either immediate daily ganciclovir maintenance therapy or deferred maintenance (8 deferred maintenance, 3 immediate maintenance). The two groups were well-matched for prior history of Pneumocystis pneumonia (PCP), visual acuity, mean age, Karnovsky score, hemoglobin, platelet count and neutrophil count at onset, as well as follow-up (4.8 vs. 5.1 months). Median time to retinitis progression was 42 days for the immediate maintenance group compared with 16 days for the deferred maintenance group, ($p = 0.07$, 2-tailed log rank test). After crossing over to maintenance therapy, patients in the deferred group had a median time to retinitis progression of 58 days compared to 16 days while not on maintenance therapy ($p=0.13$). Only 9% (10/107) of cultures obtained while patients received maintenance therapy were positive for CMV, versus 40% (8/20) of those obtained off maintenance ($p < 0.001$). For these 11 patients, median survival following diagnosis of CMV retinitis was 7 months. Nine of these 11 also had a history of PCP, with a median survival following PCP diagnosis of 8.5 months (not different from historical controls without CMV retinitis). This randomized comparative trial documents that maintenance therapy with ganciclovir delays progression of CMV retinitis and suppresses CMV shedding in AIDS patients, as compared to untreated controls.

MP.222 PHASE I TRIAL OF RECOMBINANT GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR IN ACQUIRED IMMUNODEFICIENCY SYNDROME ASSOCIATED LEUKOPENIA.

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The granulocyte-macrophage colony stimulating factor (GM-CSF) is a glycoprotein with a variety of in vitro activities including potentiation of myeloid colony growth and stimulation of leukocyte function. Because of the frequent decreased number and function of leukocytes in AIDS we performed a phase I study evaluating safety and efficacy of GM-CSF. Recombinant GM-CSF (s.a. = 4.4×10^6U/mg protein) was administered at doses of 1.3×10^3U/kg/d, 2.6×10^3U/kg/d, 5.2×10^3U/kg/d and 1.0×10^4U/kg/d to groups of 4 patients at each dose. A single IV dose was followed by a 14 day continuous IV infusion All patients were men with total peripheral WBC 3,500/ul. The drug was well tolerated with mild symptoms of headache, myalgia, and nausea. Increased liver function tests occurred in 3 patients. Recombinant GM-CSF was active in vivo with elevations in mean peripheral WBC from baseline to day 15-17 of 1850 to 4575/ul (at 1.3×10^3U/kg/d), 2675 to 8650/ul (at 2.6×10^3U/kg/d), 1900 to 8743/ul (at 5.2×10^3U/kg/d), and 2600 to 17,300/ul (at 1.0×10^4U/kg/d). No significant change in hemoglobin or platelet count was seen. The increase in WBC was mainly due to neutrophils, bands, and eosinophils with a two four-fold increase in total monocyte and lymphocyte counts. 2-10 days after discontinuation of drug the WBC returned to near baseline. Recombinant GM-CSF is active in leukopenic AIDS patients, well tolerated, and may have a clinical role as a single agent or in combination with antiretroviral therapy.

MP.223 Efficacy of BWA515U in Treatment of EBV Infection in Hairy Leukoplakia

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We investigated the effects of BWA515U, a potent acyclovir prodrug, on the clinical features and viral components of oral hairy leukoplakia (HL), an AIDS-associated lesion. We have previously shown the presence of EBV in fully replicating form in the lesion of HL using cytochemistry, electron microscopy and DNA hybridization. Fourteen patients with HL, none of whom had AIDS at the time of the study, were assigned to drug or placebo groups on a randomized double blind basis. 250 mg of BWA515U or placebo were taken orally t.i.d. for 14 days. Clinical photographs were taken at 0, 7, 14 and 28 days. Biopsies were performed at day 0 from HL lesions and at day 14 from lesions or from the site of lesions where they disappeared. 7/7 patients on active drug showed significant or complete resolution of the lesion clinically, while 7/7 receiving placebo showed no change. Histological features of HL significantly diminished in patients on active drug, while cytochemical and ultrastructural studies showed elimination or dramatic reduction of EBV infection in the active drug group only. This study shows that BWA515U was effective, on a short-term basis, in eliminating the clinical, histological and virological features of oral hairy leukoplakia.

Supported by Burroughs Wellcome and the University of California Systemwide Task Force on AIDS.

MP.224 Anti-CMV Treatment with DHPG Does not Affect HIV Antigen Levels in AIDS Patients.

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In a study of the anti-HIV effect of foscarnet in 15 patients with AIDS, HIV antigen was found in 8 before treatment, and it disappeared temporarily during and after treatment in 5 of these.

Four of the 5 patients had positive CMV culture prior to foscarnet treatment, but negative cultures during and after therapy.

PROBLEM: Since foscarnet is effective against CMV as well as against retroviral reverse transcriptase, its effect on HIV antigen could be secondary to its effect on CMV, which may be a co-factor in AIDS development and progression.

DESIGN: We have studied HIV antigens in sera from 8 patients with AIDS and CMV chorioretinitis, treated with DHPG (Syntex) for 14 days.

RESULTS: DHPG was effective against CMV clinically and virologically.
Seven patients had HIV antigen in serum.
HIV antigens did not change during DHPG treatment.

CONCLUSION: The effect nf foscarnet on HIV antigen levels is probably independent of its anti-CMV effect.

MP.225 Dose Response Study of Diethyldithiocarbamate (DTC or Imuthiol) in Patients (PTS) with ARC and AIDS.

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In previous study, DTC at a dose of 200mg/M^2 was shown to significantly improve symptoms and signs of ARC and AIDS and was shown to induce a trend towards improved prognosis. In the current study pts. with ARC or AIDS were randomly allocated (after stratification for ARC vs. AIDS, $\leq$ vs. >200 peripheral blood T lymphocytes per mm^3) to receive or not receive DTC for 16 weeks followed by a cross over to the other treatment arm on which they were again treated or not for 16 weeks. Pts. received DTC 200mg/M^2 intravenously (IV) weekly (QW)x4 wks, then 400mg/M^2 (IV) QW x4 wks, then 800mg/M^2 (IV) QW x4wks, then 800mg/M^2 twice weekly x4wks. Doses of 200 and 400mg/M^2 were non-toxic. Doses of 800mg/M^2 either once or twice per week were toxic, inducing chest pain and dyspnea, nausea and vomiting, fever and skin rash. Thus far 19 pts. have been randomized, 11 to treatment and 8 to control. Of these, 2 treated and 6 control have progressed. The treated patients progressed after 4 and 15 weeks of treatment. The treated pts. had P. Carinii pneumonia (PCP) while the 6 controls had Kaposi's sarcoma (2 pts.). PCP (2 pts.), M. avium intracellulare (1 pt.) and severe progressive weight loss (31 lbs. over 3 months) with debilitation (performance status, Zubrod, declined from 1 to 4) (1 pt.). Evaluation of blood counts, blood chemistries, T cell phenotypic markers, lymphocyte blastogenic responses to the mitogens PHA, PWM, CONA, and delayed hypersensitivity to recall antigens showed no major changes except that 8/11 treated and 1/8 control pts. showed an increase in T11 + cells at 8 weeks. These results indicate that the maximally tolerated IV dose is >400 and <800mg/M^2. The apparent difference in prognosis suggests that further controlled studies in larger numbers of pts. are warranted.

MP.226 Treatment of AIDS Based on a Combination of Synergistic Drugs

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Central to AIDS is the progressive loss of T4 helper cells by the cytopathic action of HIV, dependent on replication of the virus in infected cells. Virus-infected cells are a reservoir of virus that can spread to other normal T4 cells. Our strategy to control infectious HIV is based on three objectives: (1) inactivate extracellular virus directly, (2) inhibit replication of HIV in virus-infected cells, (3) increase the resistance of T4 cells to infection by HIV.

AME, a relatively non-cytotoxic methyl ester derivative of Amphotericin B, binds to sterols in membranes of cells and lipidenveloped viruses such as HIV. In cultures of H9 test cells infected with HIV, AME (1 to 10uM) inhibits viral replication, thus protecting H9 cells against HIV, and prevents the spread of virus from virus-infected H9. AME also prevents the spread from virus-infected lymphocytes of AIDS patients. Based on results of pretreating HIV, virus-infected H9 cells, and normal H9 cells with AME, it meets all three of our objectives. Clearly AME inactivates HIV, and in combination with Foscarnet, an inhibitor of viral reverse transcriptase, it is more effective because of synergism. Biological response modifiers are also candidates as synergistic drugs. Our results provide a rational basis for using a combination of synergistic drugs for the treatment of AIDS.

MP.227 Treatment of ARC Patients with Sodium Diethyldithiocarbamate (DTC, Imuthiol^{R}). A Multicentric, Randomized, Double Blind, Placebo controlled Trial

Members of the AIDS-IMUTHIOL FRENCH STUDY GROUP (Lyon, Paris, Strasbourg, Tours), France.

This study was designed to evaluate the clinical efficacy, immunorestorative potential and tolerance of Imuthiol in the treatment of ARC patients. Patients were selected for presence of constitutionnal symptoms and T4 cell numbers below 600/cu mm. They were randomized to be treated with either Imuthiol (10 mg/kg, once a week, oral route) or placebo capsules.

As of January 1987, 92 patients entered this study. After 4 months of treatment improvement of the clinical status was observed in 42 % of evaluable Imuthiol treated patients while 55 % were stable and 3 % worsened. In placebo group, only 8 % improved while 86 % were considered as stable and 6 % worsened. Progression to AIDS occured in 5 out of 36 placebo treated patients, but none in the Imuthiol group (N = 33). Weight loss or splenomegaly disappeared in all Imuthiol treated patients who presented these symptoms on day 0.

After 4 months, 42 % of the Imuthiol treated patients had T4 cell numbers over 600 cu mm. Recruitment of more than 350 additionnal T4 cells per cu mm over the 4 month treatment was seen in 30 % of the Imuthiol treated group. This trial will be completed before the meeting and results discussed.

MP.228 In Vivo Anti-Retroviral Properties of Recombinant Alpha Interferon in AIDS with Kaposi's Sarcoma and Healthy HIV-Seropositive Homosexual Men

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Alpha interferon is a leukocyte derived glycoprotein with anti-viral, anti-proliferative and immunomodulatory effects. It has been shown to be clinically effective in the treatment of AIDS-related Kaposi's sarcoma (KS) in 20-40% of patients and to have in vitro activity against HIV. The present study was designed to determine the in vivo anti-retroviral activity of recombinant alpha interferon in 30 AIDS patients with KS in an open trial of 35 million units of interferon daily and in 60 asymptomatic HIV culture positive homosexual men with more than 400 CD4+ lymphocytes/mm^3 in a placebo controlled trial. At this time 15 KS patients and 20 asymptomatic individuals have entered the study. Of the 9 evaluable KS patients, 5 have had a complete or partial anti-tumor response (mean CD4 count for responders = 445 vs. 101 for non-responders). Reductions in HIV-isolation were noted in 3/5 of the KS patients with an anti-tumor response and 0/4 of the non-responders. Of the 10 evaluable asymptomatic HIV infected individuals 4/5 interferon treated and 1/5 placebo treated patients became culture negative during study. Although the current sample size is too small to draw firm conclusions, it appears that alpha interferon may have in vivo activity against the AIDS virus.

MP.229 Survival of the Human Immunodeficiency Virus Under Controlled Drying Conditions on a Hard Surface.

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We determined the stability of the human immunodeficiency virus (HIV) (LAV prototype strain) after drying and storage under controlled temperature and relative humidity (RH) using the ID-50 and antigen capture assays. HIV in culture fluid (0.1 ml, ID-50=10^3) was placed on 1/2-in^2 stainless steel strips, and the strips were dried for 2 hr at 25.6°C and 28% RH in a vertical laminar-flow safety cabinet. Strips were then stored at 25°C in a desiccator jar over a saturated aqueous solution of potassium carbonate (enclosed RH=42%). We removed triplicate strips from the jar at intervals of 1,3,5, and 7 days and assayed for viable virus. At each interval, 0.1 ml of media was added to each strip for 10 minutes, and the eluent was assayed for viable virus. A liquid control was performed in parallel. The virus titer eluted from the strips was reduced approximately 1 log during inital drying, followed by a more gradual reduction over 7 days. The HIV titer held in the liquid state also dropped markedly. These results indicate that, although there is a 90% or greater reduction in titer after drying, HIV will survive drying and storage for a period of time. Survival after drying may effect future disinfectant chemical testing with this virus.

MP.230 Variation in the Humoral Immune Responses of Rhesus Monkeys (Macaca mulatta) Immunized with Formalin-Inactivated Type D Retrovirus Vaccine and Correlation with the Clinical Disease Outcome

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As part of a vaccine trial, six healthy juvenile rhesus monkeys (Macaca mulatta) were immunized with a formalin-inactivated whole SAIDS type D rhesus retrovirus serotype-1 (SRV-1) vaccine containing the adjuvant threonyl muramyl-dipeptide. Following immunization, all six animals showed antibody response against viral core and envelope proteins. The pattern of antibody response in immunized animals was unchanged in response to challenge with a potentially lethal dose of SRV-1. All immunized animals were protected from persistent viremia and remained clinically healthy. Two of six non-immunized control rhesus which received adjuvant alone, developed antibodies against core and envelope proteins following live virus challenge and exhibited only transient viremia. Four additional control rhesus failed to develop detectable antibody post-challenge and succumbed to simian immune deficiency syndrome (SAIDS).

Variations in antibody response of individual immunized animals were observed even though all received identical viral proteins. These differences may reflect the titer of antibody made by these animals to specific viral proteins. This study demonstrated that early development of specific virus-induced antibodies correlated with a favorable clinical outcome.

MP.231 Experience in Treatment of Idiopathic Thrombocytopenic Purpura (ITP) in HIV-positive Homosexuals by Perfusion of Plasma over Staphylococcal Protein A-silica (Prosorba® Columns).

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ITP is an autoimmune disease frequently found in association with HIV infection in homosexual men. In ITP platelet-associated antibodies (PAA) and/or circulating immune complexes (CIC) bind to platelets (Plt) and accelerate their destruction by the reticuloendothelial system. Recently a clinical trial was conducted to evaluate removal of PAA and CIC from plasma of ITP patients by perfusion through columns of protein A-silica. Twenty-four patients were evaluated after receiving 4-8 treatments involving absorption of 250 ml plasma. The patients presented with 50±6 x 10^3 Plt/mm^3 and elevated PAA and CIC. During treatment Plt counts in 14 patients increased 1.6-4.3 fold (mean: 2.5±0.3, P=0.04). Coincident with this effect were drops in PAA (32±9 ng IgG/10^6 Plt to 10±4 ng) and C1q-CIC (105±23 µg/ml to 60±15 µg/ml, P=0.14). Responses of 4 of these patients were transient (<2 weeks duration), while ther responses in 6 of the other 10 patients were of greater than 6 months duration. Plt counts continued to rise in these patients 1.3-4.5 fold (mean: 2.3±0.5) after termination of treatment. Plt counts and PAA and CIC levels were not altered in nonresponder patients. Serological parameters which were predictors of positive responses to treatment were PAA >10 ng/10^6 Plt (P=0.04) and C1q-CIC > 60 µg/ml (P=0.04). The results suggest that extracorporeal removal of IgG antibody and CIC from plasma modulates the autoantibody response and decreases Plt destruction.

MP.232 The Lookback Program in a High-Prevalence AIDS Region

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The lookback program has been designed to locate, inform, and test persons who received blood components prior to anti-HIV testing from donors who were later found to be anti-HIV(+). Our program provides anti-HIV testing, physician education, recipient counseling and spouse testing if requested. We have identified 513 potentially infectious components donated from June 1983 to March 1985 and have thus far located 282 recipients of whom 163 (58%) expired during hospitalization. The anti-HIV(+) rate in 53 living recipients was 77% when tested 18-42 months post transfusion; this rate did not vary over 3 seven month periods beginning in 6/83. We have not yet observed a case in which recipients from 2 consecutive donations by the same donor have been anti-HIV(-). Also, in one case, a unit of rbc was split and given to 3 infants: 2 tested anti-HIV(-) but one tested anti-HIV(+). These findings of a) a high infectivity rate of lookback donors, b) discordant anti-HIV results in recipients of the same donation, and c) the difficulty of obtaining anti-HIV results from recipients of consecutive donations lead us to recommend notifying lookback recipients as quickly as possible, rather than on a case by case basis. Counseling sessions with 19 anti-HIV(+) recipients have been vital in helping these persons to understand and cope with the information. Anti-HIV testing of 12 spouses (6 male, 6 female) has been negative despite 1 to 3 years of continued sexual contact with the anti-HIV(+) recipient. Anti-HIV testing and counseling services will increase the public health benefits of lookback programs.

MP.233 Anti-HIV Testing of Blood Donations in the United Kingdom

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Routine screening of blood donations for anti-HIV which commenced in the U.K. in October 1985 has been performed principally using the Wellcome competitive ELISA test. Donors are informed that the test will be carried out and asked to sign their agreement. Those confirmed anti-HIV positive are informed and counselled.

By the end of October 1986 approximately 2.8 million donations have been tested and 61 (0.002%) were confirmed anti-HIV positive. Of the 59 anti-HIV positive donors interviewed to date only 6 deny belonging to a recognised risk group with respect to HIV infection, the majority comprising young homosexual or bisexual men and intravenous drug abusers. Approximately 320,000 persons donating blood for the first time have been anti-HIV tested and 15 (0.004%) have been confirmed as positive. All those interviewed have admitted to being in recognised risk categories. The majority of anti-HIV positive donors attending for blood donation did so because they did not consider that the self-exclusion categories specified in the leaflet issued to all donors applied to them since their homosexual activity or drug abuse had terminated several years ago. A revised leaflet has now been issued to donors in an attempt to resolve such misunderstandings.

Four confirmed anti-HIV positive donors had been tested previously. One was found to give repeatedly equivocal results and the donation was not used. Of the remaining three found anti-HIV negative one is known to have led to seroconversion following transfusion of products from the donation to two patients.

MP.234 Inhibition Enzyme Immunoassay for Determination of Anti-HIV Specificity

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Only a small proportion of donor blood found repeatable reactive in currently available commercial enzyme immuno assays (EIA) is specific for anti-HIV when tested by Western blot (WB) assay. WB assay is subjective and prone to technical variation and is therefore not suitable for routine use as a confirmation test. We have developed an Inhibition EIA that utilizes biotinylated human IgG anti-HIV and an antigen coated solid phase from Abbott or Genetic System tests for anti-HIV. The Inhibition EIA is based on competition-inhibition format and is designed to be used in the field in conjunction with the commercial test in use for screening of donors. Using Inhibition EIA we successfully identified as positive 53 of 55 WB positives and also found 64 of 65 WB negatives as nonreactive. WB negative samples included 32 that were repeatably reactive in Abbott EIA. We tested additional 166 specimens that were repeatably reactive in Abbott EIA but demonstrating atypical or "indeterminant" band patterns in WB. Only 1 was found reactive in Inhibition EIA. This sample was later found to be WB reactive on retest. Inhibition EIA is a simple, objective and reliable substitute for WB for routine determinantion of anti-HIV specificity.

MP.235 Removal of human immunodeficiency virus (HIV) by ultrafiltration

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We intend to propose a new method to remove HIV perfectly from a desired solution such as plasma. As a filter, the regenerated cellulose membranes having various mean pore sizes were prepared from the cupurammonium solution of cellulose through the microphase separation method. After the filtration of HIV preparation with these membranes, we evaluated the infectivity of HIV in both filtrates and filtrants through the assays for HIV-induced cytopathic effect (CPE), immunofluorescence method for expression of HIV-specific antigens and a plaque assay for quantitation of biologically active virus using MT-4 cells. When the pore size of the membrane determined by the water filtration rate method was smaller than 30 nm, neither CPE nor fluorescnet cells were detected in MT-4 cells cultured with the filtrates five days after culture, whereas in the cells with filtrants, remarkable CPE was observed and all cells were fluorescent three days after culture. Moreover, under such filtration conditions, no plaque was formed with the filtrates although the titer of HIV in the filtrants showed 10^6 level of plaque-forming units per ml. In addition, the novel porous polymeric membrane was found to scarcely absorb protein molecules.

MP.236 Traps of HIV-Serology: Independent Changes in Sensitivity and Specificity of ELISA Kits

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As a National Reference Laboratory for blood donor screening and transfusion-related HIV-infection, we have tested 1374 serum samples for the presence of HIV antibodies. More than 150 repeatedly ELISA positive samples were found by us or sent to us for control. Out of them, anti-HIV positivity could be confirmed by IFA and/or WB tests in 39 samples. 118 samples, however, were found to be false-positive. Using deep-frozen aliquots of these sera, we have compared sensitivity and specificity of different batches of 6 different commercial anti-HIV ELISA kits. A mathematically-evaluated serum dilution method was used for the sensitivity measurements. Two types of changes were observed at repeated determinations: a.) a significant inter-batch and even inter-box sensitivity difference was found with some kits, relative sensitivity of the different kits also changed, b.) reactivity of the plates for true-positive and false-positive sera independently changed among different batches of the same kit: while reactivity for true-positive sera was constant, a significant decrease or increase in reactivity for false-positive sera were found. These observations point to poor reproducibility of some commercial kits which can cause serious difficulties in screening laboratories.

MP.237 Evaluation of an Anti-HIV Screening Test Using HIV env Specific Synthetic Oligopeptides

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A research ELISA test in which microtiter wells were coated with synthetic peptides from the env region of the human immunodeficiency virus (HIV) was evaluated for accuracy. Serum samples previously tested for anti-HIV with licensed ELISA reagents and the Western Blot method were selected for testing with the env peptide assay. The assay detected 25/26 (96%) samples that were repeatedly reactive (RR) by ELISA and confirmed anti-HIV specific (p24 and gp41 bands) by Western Blot. Two (2) patient samples that showed reactivity to the gp41 band only were reactive on the env peptide assay. Of 35 samples from healthy individuals that were RR by ELISA but reactive only with the p24 band on the env peptide assay 33 (94%) were non-reactive. The peptide assay correctly identified as negative > 98% of 212 samples from blood donors who were non-reactive for anti-HIV by ELISA and Western Blot. These preliminary data indicate that the env specific peptide assay may provide a sensitive and specific alternative to ELISA screening tests which use whole viral lysate.

MP.238 Prevalence of Antibodies against Various Epitopes of Envelope (gp 120,gp41) and GAG Proteins of HIV in AIDS Patients.

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Peptides corresponding to various conserved regions of envelope and gag were cloned and expressed in E. coli. Fusion peptides that contain portions of gag and envelope were also made. In addition, small peptides (10-30 amino acids) corresponding to various regions of gp 120, gp 41 and tat were synthesized by solid-phase peptide synthesis. Recombinant proteins and synthetic peptides were tested for their immune reactivity against normal sera (600 samples) and HIV antibody positive sera (597 WB+ samples). We have identified several highly antigenic epitopes of envelope (amino acid sequences 58-68 and 487-511 of gp 120, 578-608 of gp 41), gag and tat that may be useful in early identification of HIV infection. Peptides corresponding to these antigenic epitopes were used as HIV antigen in an ELISA test for antibody. One of these fusion proteins showed 100% sensitivity and 100% specificity when used as HIV antigen in a bead-EIA test for HIV antibody developed at Roche. The data on a) purity of HIV peptides, b) antigenic epitope-analysis of gp 120 and gp 41 and c) development of a simple and accurate test for HIV antibody will be presented.

MP.239 Effects of Drying on the Human Immunodeficiency Virus (HIV) Diluted in Heparanized Blood, Serum or Media.

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We assessed survival of HIV after drying the virus in tubes and in covered tissue culture plates. In both, drying required several hours. In the first, tubes containing 0.1 ml of virus in media were dried under vacuum in a desiccator and maintained dry until tested.

	ID-50		
Day	4°C-Liquid	Room temperature-Liquid	Room temperature-Dried
0	$10^{5.7}$	$10^{5.7}$	$10^{5.7}$
1	$10^{4.8}$	$10^{3.5}$	$10^{3.9}$
3	$10^{7.0}$	$10^{1.9}$	$10^{2.4}$
5	$10^{3.9}$	$10^{2.1}$	$10^{3.9}$
6	$10^{4.1}$	$10^{1.4}$	$10^{2.1}$

In another set of experiments, virus diluted in heparinized blood, serum (both negative for HIV antibodies) or media (RPMI +10% FCS, +10% IL2) was plated into 24 well plates, which were covered and allowed to dry overnight at room temperature (RT) or 37°C. The dried matrix was then rehydrated and the ID-50 titer determined. In 3 experiments, no virus was recovered after drying at 37°C.

	ID-50 before drying/after drying at RT		
Matrix	Exp.1	Exp.2	Exp.3
Media	$10^{3.8}/10^{3.2}$	$10^{3.9}/10^{3.0}$	$10^{4.0}$/Not Done
Serum	$10^{4.8}/10^{3.4}$	$10^{3.8}/<10^{1.0}$	$10^{3.0}/<10^{1.0}$
Blood	$10^{4.3}/<10^{2.0}$	$10^{5.0}/<10^{1.0}$	$10^{3.8}/<10^{2.0}$

These results suggest that survival of HIV following drying at room temperature can vary.

MP.240 Improved Immune Studies in HIV Antibody-Positive Hemophiliacs: Association With Decreased Alloantigen Bombardment.

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We have previously presented data to indicate that the immune defect in hemophilia is multifactorial. Contributors include: HIV infection, other viral infections, and exposure to a large array of alloantigens found in clotting factor concentrates. Factor VIII:C purified utilizing a mouse monoclonal antibody to FVIII:VWF was used exclusively for 6 months to treat hemorrhages on a demand basis in 7 HIV antibody-positive patients with severe hemophilia A. This therapeutic material has approximately 3,000 x the specific activity of previously available products. Laboratory assessments included ELISA assay to detect antibody to mouse protein and immunological data including quantitative T cell subsets and skin testing on each patient on entrance to the study, at 1 month, 3 months and at conclusion in order to ascertain whether immune function in these patients would improve with the use of purer factor concentrate.

Six of seven patients did not develop significant levels of anti-mouse IgG antibody. (One patient had a rheumatoid factor which interfered with the ELISA assay for anti-mouse antibody and thus its presence could not be assessed.) There were no adverse reactions to the material, and hemostatic efficacy was judged as excellent. There were no significant changes in quantitative T cell subsets. Three out of six patients lost their previous total skin test anergy and two other patients increased the number of antigens to which they reacted. This concentrate proved to be safe and efficacious, to have excellent half-life, and to be associated with apparent improvement in the immune response.

MP.241 Risk of Human Immunodeficiency Virus (HIV) Infection for Recipients of Blood From Donors Positive for HIV Antibody

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We evaluated recipients of previous blood donations from donors who were later found positive for HIV antibody by enzyme immunoassay, but negative on Western blot assay (EIA+/WB-) and from donors positive by both tests (EIA+/WB+). Donors were evaluated by HIV culture and date of the EIA positive donation. Of 109 donors of EIA+/WB- donations, 62 (57%) had 174 previous donations split into 264 components. Of 180 recipients investigated, 94 (52%) were dead; of the 86 who were alive, 69 (80%) were tested for HIV-antibody and 3 (4%) were positive. Two seropositive recipients had clotting disorders and the other had previously received a large number of transfusions. Of 101 donors of EIA+/WB+ blood, 45 (45%) had given 94 previous donations split into 120 components. Of 83 recipients investigated, 44 (53%) were dead; of the 39 who were alive, 31 (79%) have been tested for HIV antibody, and 11 (35%) of them were positive. Seropositive recipients and seronegative recipients were similar for the time interval between their transfusion and the donor being found EIA+/WB+ (14.6 months vs. 15.2 months). Also, both groups of recipients from these donors received about the same proportion of red cells (69% vs. 60%) and had no significant difference in likelihood of receipt of blood from HIV-culture positive donors (4/7 vs. 6/7). Four of six heterosexual partners of antibody-positive recipients were tested for HIV antibody; none were positive. Previous recipients of blood from EIA+/WB+ donors are at significant risk for HIV infection. Serologic testing for HIV infection of other multiply transfused persons may be indicated.

MP.242 Long-Incubation HIV Infection in a Donor, Recipient and Children

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A case of transfusion-acquired HIV infection (TA-HIV) demonstrated a long disease incubation period in the implicated donor, the transfusion recipient, and her secondarily-infected children, suggesting that the involved HIV isolate had reproducible, though unusual, infectious disease characteristics:

In 1978, a woman received 4 RBC units during her first pregnancy. Two years later she had a second child with failure to thrive. By age 5, the child developed adenopathy, tested positive for HIV antibody, and was diagnosed with ARC. When the mother, husband and firstborn child were also found to be antibody positive, the case was investigated as possible TA-HIV with secondary infection of both children and the husband. Three of the donors were unlikely sources of infection. The fourth - a 28 year old man - was found among the CDC-listed AIDS cases using a confidential coded identifier. He had become ill in 1985 and died 9 months later with AIDS. The firstborn child has since developed ARC at age 8; both parents remain asymptomatic.

The donor was infectious and asymptomatic for a minimum of 7 years. The recipient has been silently infectious for 8 years and her first child developed symptoms of congenital infection at age 8. This case represents an early instance of TA-HIV and indicates the need to consider transfusions even earlier than the 5 year incubation limit presently used by Red Cross to define involved donations in reported TA-HIV.

MP.243 CLINICAL STUDIES OF A SYNTHETIC PEPTIDE BASED HIV ANTIBODIES TEST KIT

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We have developed an EIA kit for the detection of HIV antibodies using synthetic peptides representing highly antigenic epitopes of the gp41 envelope and p24 core proteins of HIV as the solid-phase immunoadsorbent. The total assay time is 45 minutes. An evaluation of this kit was conducted in three geographically distinct blood centers and a hospital laboratory with abundant patient populations known to be at risk for the disease. Over 6200 samples have been evaluated from a random population resulting in 0.65% initially reactive (IR); 54% of the IR samples were repeat reactive (RR) giving rise to a RR rate of rate of 0.35%. Approximately 10% of the IR were positive on the Western blot (WB) analysis. With the assumption of 100% prevalance of antibodies to HIV in AIDS patients, the sensitivity is estimated to be 100%. Thus the specificity, sensitivity and the overall efficiency of the test kit is 99.71%, 100% and 99.72% respectively. Seroconversion studies from twenty patients with over 200 specimens collected over a closely spaced period are compared with this kit and other licensed kits and with WB analysis. Our kit demonstrates better sensivity in detecting HIV antibodies in all patients. Five patients even gave positive signals prior to that detected by WB analysis. RR samples, tested by other licensed HIV test kits, have been studied in all three blood centers. All of the 580 WB positive samples are reactive with our test and only three of the 125 WB negative samples are reactive. All these WB negative specimens are RR by at least one other licensed test kits.

MP.244 Screening Test Allowing Simultaneous Detection of HIV Antibodies and HBsAg

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A combination HBsAg/anti-HIV enzyme immunoassay (EIA) has been developed allowing simultaneous detection of both HBsAg and antibodies against HIV in sera and plasma. In this combination assay, polystyrene beads coated with recombinant DNA derived (rDNA) HIV antigens (ENV and CORE) and antibodies against HBsAG (anti-HBs) are incubated with specimen, washed, and then reacted with a solution containing rDNA HIV antigens and anti-HBs conjugated to horseradish peroxidase (HRPO). This assay requires no sample dilution because a specific antigen conjugate is used rather than an anti-human antibody conjugate. Results indicate that this assay is up to 64 fold more sensitive than currently licensed anti-HIV tests and is equivalent in sensitivity to Auszyme II. 68 AIDS/ARC sera, 250 anti-HIV positive sera, and 96 HBsAg positive sera were all reactive in this assay. Less than 0.1% of the 4,000 random blood donors tested were repeatably reactive in the combination assay.

Results from this assay do not allow discrimination or differentiation between HBsAg and anti-HIV positivity. Use of the combination assay may eliminate the need to screen blood with two distinct immunoassays.

MP.245 HIV Antibody and Virus Detection in a Cohort of Haemophiliacs.
P. SIMMONDS*, ROBERT J.G. CUTHBERT**, F.A. LAINSON*, J.F. PEUTHERER*, C.H. STEEL***, C.A. LUDLAM**. *Dept. of Bacteriology, Edinburgh University. **Dept. of Haematology, Royal Infirmary of Edinburgh, ***MRC Clinical and Population Cytogenetics Unit, Western General Hospital, Edinburgh.

The study group comprises 32 haemophiliacs who were exposed to factor VIII contaminated with HIV in 1984. 18 patients in this group developed antibody to HIV, the others have remained seronegative. Serum samples are available from before exposure to the present day. In this work we compare serological markers of viral infection, and relate this to the detection of antigen in serum and the isolation of HIV from peripheral blood lymphocytes. Serological tests for the detection of HIV antibody include immunoblotting, indirect immunofluorescence, Abbott EIA for antibody to core and envelope proteins, and Wellcozyme and Dupont EIAs. Antigen detection is by Abbott EIA an Dupont RIA.

Antibody detection tests provide accurate determination of the time of seroconversion. There was no significant difference in sensitivity between the tests demonstrable in this study. However variation was observed between individuals in the development of reactivity to the core bead in the Abbot EIA. Futhermore, the pattern of bands in immunoblotting varied with time following seroconversion. Antigen can be detected before seroconversion in some of the HIV-infected haemophiliacs. A proportion of these remain positive for antigen for a time following seroconversion. Virus isolation studies have demonstrated the presence of virus in 2 of 15 seropositive individuals examined to date.

MP.246 The Relationship of Antibody to HIV, Age, Sex and Treatment to Lymphocyte Subsets in Congenital Clotting Disorder (CCD) Patients
MARY ANN FLETCHER*, THE TRANSFUSION SAFETY STUDY GROUP* **, *The University of Miami School of Medicine, Miami, FL, ** other participating institutions.

The Transfusion Safety Study Group (TSS) is a multifaceted cooperative investigation of factors modifying the occurence and expression of transfusion- transmitted infections. Lymphocyte subset data on 608 patients with CCD show lower T4/T8 ratios and numbers of T4+ cells and higher counts of T8+ and T11+ cells in the 59% who were anti-HIV (+) (p=.01 to .0001). These anti-HIV (+) patients had more T8+ cells expressing the class II activation marker I2 (p=.0001), but fewer T11+ cells with the alternate pathway T cell activation marker TA1 (p=.0001). They also had an increase in the suppressor inducer subset 2H4 (p=.0001). However, patients <10 years had significantly elevated 2H4+/T4+, and lower 4B4+/T4+ subset (p=.0001), as well as elevated lymphocyte counts (p=.0001) and T8+, T4+ and T11+ cells (p=.05) regardless of anti-HIV status, compared to older patients. Among anti-HIV (-) patients, females had significantly higher %T4+, %T11+ cells and T4/T8 ratios and lower % of T8 cells and I2+/T8+ cells (p=.05 to .0001). Within the group of anti-HIV (+) patients, and also within the anti-HIV (-) group, %T8+, %T11+ and I2+/T8+ cells were higher and T4/T8 ratios lower in those patients treated with concentrates rather than unpooled components (p=.05 to .0001).

In summary, significant differences in lymphocyte subsets were found when comparing patients with regard to anti-HIV status, but age, sex and treatment also affected these observations. Possibly, the T cell subset differences detected affect the susceptiblity to and progression of HIV infection in CCD patients. (Supported by Contract No. N01-HB-4-7003 of the National Heart, Lung and Blood Institute.)

MP.247 Lookback: The Greater New York Blood Program Experience
SUZANNE GAYNOR, J. PINDYCK, New York Blood Center, New York, N.Y.

Lookback, the policy of tracing recipients of previous transfusions from currently anti-HIV positive blood donors, was implemented in the New York region in October, 1986 after lengthy deliberations. Due to the size of the region served, (232 hospitals in N.Y.& N.J.) and the number of anti-HIV positive donors (609 on October 1st) the complexity of the undertaking required careful planning. The Blood Center established a Task Force representing hospitals, physicians, attorneys and patients to advise on the optimal way for hospitals and the blood center to proceed. Guidelines for hospitals and written information to assist those notifying the patient were developed. With support from community service agencies, a four hour training program for hospital personnel was developed, covering AIDS epidemiology, screening, confidentiality and counseling issues. The seven sessions held to date have been attended by 227 physicians, nurses, social workers and laboratory personnel. These sessions will be continued and expanded to meet hospital needs.

A microcomputer system generates product traces and forms to report outcome of the hospital search. Information on 614 products dating back to January, 1983 has been distributed to 121 hospitals and this process will be ongoing. To date, 158 responses from 1984-86 period have been received; 102 patients (71%) are deceased. Of the 42 living patients, 22 were screened by the N.Y.B.C. ELIZA, Western Blot and IFA are done on all samples. Eleven patients, or 50% are Western Blot positive. Six patients were tested elsewhere; three (50%) are Western Blot positive. Thus, this very preliminary data appears to validate the decision to undertake the Lookback program.

MP.248 Antibody Reactivity To HIV Proteins As Measured By Commercial Western Blot (WB) Assays
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The ability to distinguish reactivity of serum antibodies to individual HIV proteins was studied by examining a series of patient sera samples, each assayed with several different commercial Western Blot (WB) tests. Samples were first assayed in serial dilutions by commercial ELISA tests. Results were confirmed by radioimmunoprecipitation assays (RIPA). In most instances, the WB assays showed reactivity to HIV antigens at titers significantly higher than those found by commercial ELISA assays. However, detection of antibodies to specific viral antigens varied considerably between the WB tests. This was particularly true for detection of antibodies to the high molecular weight viral glycoproteins, gp160 and gp120. Some commercial kits appeared deficient in these antigens and were unable to detect antibodies to them. In contrast, at least one WB assay was able to detect the viral glycoproteins at titers beyond the end point for detection of p24, the major viral core protein. When specimens testing negative or indeterminate for anti-HIV antibodies by ELISA were tested by WB some kits occasionally showed non-viral reactive bands or gave a non-specific dark background which confused interpretation. Moreover, different band patterns were often found for the same serum dilutions with different kits presumably as a result of having different relative viral antigen concentrations on the strips. Our study demonstrates clear differences in band patterns and sensitivity between kits especially in the high molecular weight regions. Differences were noted in the correlation between RIPA and some of the WB kits at the 160,000 and 120,000 MW glycoprotein bands.

MP.249 Clinical and Laboratory Follow-up of Asymptomatic Blood Donors with only Anti-Core Antibodies
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The clinical relevance of anti-HIV p15,p24,p55 antibodies, single or associated, is still controversial. We report the results of a clinical and laboratory follow-up of 59 subjects displaying such an artibody pattern.

The subjects were asymptomatic blood donors, found to be positive at ELISA screening (DuPont, USA) and confirmed by Western blot (WB) using in parallel reagents supplied by DuPont and by Diagnostics Pasteur (France) or Bio-Rad (USA). All subjects but 5 denied risk factors for HIV infection. CD4/CD8 ratio by cytofluorometry (Spectrum III, Ortho Diagnostic Systems, USA), skin testing by recall antigens (Merrieux, France) and screening for lymphocytotoxic antibodies were also performed. Clinical evaluation, Western blot analysis and CD4/CD8 ratio were repeated at 3-month-intervals for 5-21 months (median 9). Results are summarized in the table.

SUBJECTS		Inverted	Positive lymphocyte	Changes during follow-up	
WB pattern	No.	CD4/CD8	abs screening	clinical	WB pattern
anti-p15 alone	16	1/ 8	13/15	0/16	1/16(p15,45,55)
anti-p24 alone	14	1/ 9	9/13	0/14	1/14(p24,55)
anti-p15,24,55	29	3/17	11/15	1/29(AIDS)	2/29 complete pattern (p24,45,55,64)

Sexual partners of 19 subjects were also examined and found to be seronegative except in 2 cases. In conclusion, the above results suggest that the clinical relevance of anti-p15.p24.p55 is generally low at least in the follow-up period considered, but not nil. The unexpectedly high frequency of anti-lymphocyte-antibodies in the examined subjects deserves further investigations.

MP.250 Risk of HIV transmission by blood components during the two year period prior to institution of routine anti-HIV screening.
JOHN THOMAS[1], R. BOWMAN,[2,4,5] F.S. RHAME[1,2,3], 1-School of Public Health, 2-Dept of Lab Med and Path, 3-Dept of Medicine, 4-Blood Bank, U Minnesota Hosp, U Minnesota Minneapolis, 5-American Red Cross St. Paul Regional Blood Center, St. Paul, MN.

To assess the HIV transmission risk due to transfusion of blood components prior to 3/85, we studied multiply transfused patients. Between 3/16/83 and 3/28/85, 1201 persons received 30 or more donor unit exposures (DE) at U MN Hosp. 541 persons were excluded: hospital records indicated 521 had died without an anti-HIV serology, attending physicians denied permission to contact 9 patients, 11 hemophilia patients had received coagulation factor concentrate. 660 patients (approximately 98,000 DE) were further evaluated. 2 were known to be HIV infected: one was tested because of lymphadenopathy, one because of a look back study; neither had other HIV risk activities. 36 patients (10,848 DE) had been anti-HIV tested (presumably because of their transfusion history) of whom 12 (5,997 DE) were hemophilia patients who had not received coagulation factor concentrate; all 36 were anti-HIV negative. Letters were sent to the remaining 622 evaluated patients requesting serum for anti-HIV testing. 200 recipients (21,686 DE) participated: 2 were anti-HIV positive. Both denied other HIV risk activities; stored serum taken from both just prior to the transfusions was anti-HIV negative. Donor evaluations are under way.

Of 236 multiply transfused persons (32,534 DE) tested because of their transfusion history, 2 had become HIV infected. Persons receiving multiple donor exposures in the period prior to anti-HIV screening of donor blood may be at enough risk of HIV infection to warrant routine anti-HIV screening.

TUESDAY, JUNE 2

Plenary Session II

T.1.1 Epidemiology and Prevention of AIDS and HIV Infection in the United States

JAMES W. CURRAN, AIDS Program, Center for Infectious Diseases, Centers for Disease Control, Atlanta, GA.

Between June, 1981 and January 26, 1987, 29,582 cases of AIDS were reported to the Centers for Disease Control (CDC) from 50 States and territories and the District of Columbia. Nearly 17,000 (57 percent) of these patients are reported to have died. (70 percent were under 40 years of age, 93 percent were men, and 73 percent were identified as homosexual or bisexual in orientation.) Nearly 13,000 cases of AIDS were reported in 1986, a 58 percent increase over 1985 reports. The largest percent increases were among heterosexual men and women and in geographic areas other than New York, California, and Florida. Among 6,000 cases reported in heterosexual men and 2,000 cases in women, 68 percent and 51 percent were directly associated with IV drug abuse. Over 22 percent of cases in women and 2 percent of cases among heterosexual men were reported as contacts of persons with known HIV infection or in a group at increased risk. Updated statistics and results of collaborative studies and prevention efforts will be discussed.

T.1.2

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

T.1.3 Aids Epidemiology, Impact, Prevention and Control: The World Health Organization Perspective.

Jonathan Mann, World Health Organization, Geneva, Switzerland.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

Plenary Session III

T.2.1 Vaccination against Retroviruses

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The greatest degree of experience in vaccinating against retroviruses is with Feline Leukaemia Virus (FeLV).

Classical attentuation procedures cannot be used as the virus promoters and enhancers of the long terminal repeats are potentially oncogenic by insertional mutagenesis. Serious consideration has therefore been given to subunit vaccines, cell membrane preparations and recombinant virus constructs. The first effective vaccines to give 100% protection were cells killed by paraformaldehyde and adsorbed to aluminium hydroxide. This stressed the importance of the presentation of an antigen array; the effective epitope is on the surface spike glycoprotein, gp70 and the effector arm is virus neutralising antibody. The virus gp70 is highly expressed on the surface of infected cells. Preparations of killed virus and adjuvanted free glycoprotein have been unsuccessful as have preliminary attempts to immunise with env-gene containing vaccinia recombinants. A highly successful vaccine has been achieved using ISCOMS. Results, both laboratory and field, will be presented. A similar prototype vaccine using HIV has been made and used in monkeys and apes. It proved safe in a long term trial and induced anti-HIV antibodies. Results will be shown and discussed.

T.2.2 Immunopathegenic Mechanisms and Immune Response in HIV Infection.

Anthony S. Fauci, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

T.2.3 CHEMOTHERAPY OF HIV INFECTIONS. Samuel Broder, M.D., National Cancer Institute, National Institutes of Health, Bldg. 10, Room 12N214, Bethesda, MD 20892. We have found that with the ribose moiety of the molecule in a 2',3'-dideoxyconfiguration, almost every purine or pyrimidine suppresses HIV replication in vitro. However, dideoxythymidine had less activity in our system than the others. Interestingly, the substitution of an azido group or a cyano at the 3'-carbon in place of a hydrogen significantly restored the anti-retroviral effect of the dideoxythymidine derivative. An analysis of five adenosine congeners, which differed only in the sugar moiety, revealed that reduction (an absence of the hydroxyl groups) at both the 2' and 3' carbons of the ribose was necessary for an antiviral effect, and an additional reduction at the 5'-carbon (the site of phosphorylation after entry into the target cells) nullified the antiviral activity. Recent studies suggest that nucleosides which are in a 2',3'-dideoxy-configuration may have the capacity to inhibit diverse retroviruses (both human and animal). The key determinant of anti-retroviral effect seems to be the capacity of the target cell to anabolically phosphorylate the nucleoside analogue; a lack of effective anabolic phosphorylation will make a retrovirus appear to be drug resistant. Clinical trials with AZT (the azido analogue of dideoxythmidine) have shown good oral bioavailability and penetration across the blood/brain barrier in patients with AIDS. Recent studies have shown that AZT can confer a significant survival advantage to patients with AIDS compared to placebo. AZT can provide significant clinical benefits to certain adults and children with AIDS-related neurologic disease. Another dideoxy-analogue (dideoxycytidine) is now in phase I testing and preliminary results suggest that it may have less bone-marrow suppressive effects. The observations serve as a stimulus for further clinical research and provide some measure of optimism in the search for successful future strategies in treating AIDS.

Epidemiology—Serology

T.3.1 Detecting Antibody Against Human Immunodeficiency Virus (HIV) During Early Infection using the Western Blot (WB), Radioimmunoprecipitation Assay (RIPA), and Synthetic pENV9.

ALFRED J. SAAH*, H. FARZADEGAN*, T.H. LEE**, S.R. PETTEWAY***, C.R. RINALDO*, J.P. PHAIR*, J.L. FAHEY*, *The Multicenter AIDS Cohort Study (MACS), Bethesda, MD, **Harvard School of Public Health, Boston, MA, ***Central Research and Development Department, E.I. du Pont de Nemours & Co, Inc., Wilmington, DE, USA.

A current concept of the serological response to HIV infection in man is that antibodies to HIV core antigens (p55, p24, p15) are detectable earlier than antibodies against envelope antigens (gp160, gp120, gp41) during initial stages of antibody production following natural infection. As a related matter, reactivity to synthetically produced envelope antigens during early infection is relatively unstudied. Sera from 37 gay/bisexual men in the MACS showed reactivity predominantly to core antigens in the WB that was established as occurring early during seroconversion. Longitudinal specimens from these men showed a WB band pattern that clearly confirmed infection with HIV. 30 of the 37 early sera totally lacked antibody to gp41 in the WB; of these, 27 (90%) were reactive for anti-gp120/160 in the RIPA. When the same 30 sera were tested against pENV9 in an ELISA format, 27 (90%) were also found to be positive. One serum that was negative by RIPA was positive by pENV9 and another that was negative by pENV9 was positive by RIPA. Both discordant sera had solitary strongly reactive p24 bands in the WB.

We conclude that, given HIV infection, almost all sera that are reactive only for anti-core in the WB also contain anti-envelope antibodies. Further, the pENV9 assay seems to be equivalent to the RIPA for detecting early antibodies to envelope proteins.

T.3.2 Reversion of HIV Serology from Positive to Negative in Gay/Bisexual Men Who Remain Healthy.

MICHAEL A. POLIS, B.F. POLK, J.P. PHAIR, C.R. RINALDO, P. NISHANIAN, A.J. SAAH, et al., The Multicenter AIDS Cohort Study (MACS), NIH, Bethesda, MD, USA

Five of 4955 participants in the MACS have been identified as showing reversion of their HIV ELISA test results from positive to negative, with corresponding changes in the Western blot. Western blots were performed simultaneously from serial frozen séra. Genetic relatedness of the longitudinal sera was confirmed by evaluation of 7 serum proteins using the same serum aliquots that were used for the immunoblotting.

Serum specimens were drawn at 6 month intervals over a period of 6 to 18 months after the initial positive test. Three participants had multiple bands by Western blot that disappeared at the next sampling 6 months later (n=2) or gradually over 12 months (n=1). The remaining two subjects did not become completely negative by immunoblot but showed progressive fading of bands over a 12 month period. Both of these men lost detectable antibody to p24 and gp41 but retained other bands, one for p15 and p53, and the other for p55 and p64.

Whether these subjects have ever been infected with HIV remains to be determined by culture. All sera were negative for p24 using an antigen detection test. Clinical (lymphadenopathy, fever, diarrhea, weight loss, fatigue, and thrush) and laboratory features (hematocrit and platelet, total lymphocyte, T-helper and T-suppressor counts) were not significantly abnormal and did not appear to parallel changes in the Western blot in the 5 subjects.

A case/control study is underway to help determine the cause of the observed reversion and the significance of this phenomenon.

T.3.3 High HTLV-III/LAV Neutralizing Antibody Titers Correlate with Better Clinical Outcome.

M. Robert-Guroff, J.J. Goedert, A. Jennings, W.A. Blattner, and R.C. Gallo. National Cancer Institute, Bethesda, MD, USA.

To investigate HTLV-III/LAV neutralizing antibodies and protective immunity we studied serum samples collected prospectively between 1982 and 1985 from 34 homosexual males. By ELISA, 26 subjects were sero-positive for HTLV-III/LAV in 1982. Of these, 13 progressed to AIDS and 13 remained healthy. Eight subjects seroconverted during the study. One developed AIDS, and 7 remained healthy. Neutralization of cell-free virus infection of H9 cells by serially diluted sera was assessed. Infection was monitored by immune fluorescence assay for viral p24 expression, and titers, serum dilution^{-1} at which viral infection was 60% of the control, were determined. Geometric mean titers (gmt) of neutralizing antibody in the healthy seroconverters increased from 13 in 1984 to 49 in 1985. The healthy seroprevalent individuals exhibited consistently high gmt's: 121 in 1982, 99 in 1983, 125 in 1984, 281 in 1985. Progressers to AIDS had significantly lower gmt's beginning 2 years prior to AIDS diagnosis. The gmt's 3, 2, and 1 year before, and 1 year after AIDS diagnosis were 57, 36, 20 and 22, respectively. These results show that neutralizing antibody levels rise slowly, but may remain at relatively high levels for several years in association with a healthy clinical status. In contrast, consistently low neutralizing antibody titers signal poor prognosis. The influence of higher titers on long term survival should be further evaluated.

T.3.4 Anti-gag Antibodies to HIV; Association with Neutralization and Clinical Outcome in Cohorts of Homosexual Men

JONATHAN WEBER*, P. CLAPHAM*, R. WEISS*, D. PARKER**, R. CHEINSONG-POPOV**, et al., *Chester Beatty Laboratories, Institute of Cancer Research, London, **Wellcome Foundation Laboratories, Beckenham, Kent.

Sequential sera from 48 subjects infected with HIV-1 were examined prospectively over a 36 month period for neutralizing antibody titre, and titre of anti-gag antibody (p 24), and anti-env antibody (gp 41). Neutralization was measured by the VSV pseudotype assay, and the gag and env titres were assayed by ELISA on recombinant antigen, and by radioimmuno-precipitation. Data were analysed in terms of clinical outcome of the cohort at 36 months. Subjects who remained asymptomatic over 36 months had a significantly higher titre of antibody against p 24, compared to subjects developing AIDS or ARC. There was a trend towards increasing neutralizing titres over time in the asymptomatic group, but this was non-significant. The titre of gp 41 was constant over time in all subjects. There was no independent association between p 24 titre, and neutralizing titre, which implies that the possible protective action of anti-p 24 is not mediated through neutralization. However, three of six anti-p 18 monoclonal antibodies show weak neutralizing activity against HIV (ARV-2). Further analysis of these cohorts for the relationship between p 18 and neutralization will be present. As there is no evidence of a humoral response to p 24, the role of p 24 as a target for cellular cytotoxicity will also be presented.

T.3.5 HIV antigenaemia precedes the developement of AIDS or ARC in patients with HIV infection.

COURT PEDERSEN*,C.M.NIELSEN**,B.F.VESTERGAARD*,*,J.GERSTOFT*,K.KROGSGAARD*,J.O. NIELSEN*. *Department of Infectious Diseases,Hvidovre Hospital,**Statens Seruminstitut,Copenhagen,Denmark.

Sequential serum samples from 33 patients with HIV antibodies were tested for the presence of HIV antigen using a newly developed double antibody biotin-avidin amplified sandwich ELISA (Statens Seruminstitut,Copenhagen).

HIV antibodies were in all patients demonstrated before December 31st 1985, and none of the patients had AIDS or the AIDS related complex (ARC) by that time.Serum samples were collected every fourth month.The median follow up time was 38 months (range 24-65 months).

During the time of observation,HIV antigenaemia developed in 16 patients.Five patients in whom HIV antigenaemia appeared developed AIDS,and 3 patients developed ARC.In contrast,only 1 patient without HIV antigenaemia developed AIDS.

HIV antigenaemia preceded the onset of AIDS by 7 to > 25 months,and the onset of ARC by 3 to > 24 months.

At the end of the follow up period (January 1987),15/16 patients with HIV antigenaemia had a decreased number of T-helper/inducer cells in peripheral blood (< 0,5 x 10^9/l).In contrast,only 7/17 patients without HIV antigenaemia had a decreased number of T-helper/inducer cells.

In conclusion,the study indicates that the developement of AIDS or ARC in most patients with HIV infection is preceded by HIV-antigenaemia .Thus,HIV antigenaemia signifies active viral infection with resultant immunodeficiency, and later the onset of AIDS or ARC.This may be of importance,when patients are selected for treatment with antiviral agents.

T.3.6 HIV ANTIGENEMIA AND AIDS

JOHN P. PHAIR, J. CHMIEL, C-B WALLEMARK, W. WU, J. HUPRIKAR, Northwestern University Medical School and Howard Brown Memorial Clinic, Chicago, IL, U.S.A.

The frequency of human immunodeficiency virus antigenemia (HIVAg) was determined using plasma obtained at semiannual intervals (1984-1986) from 121 homosexual or bisexual men enrolled in a prospective study of the natural history of HIV infection. By design the study contained 38 participants persistently negative for HIV antibody, 23 seroconverters and 60 men seropositive at entry, including 27 who have developed AIDS. Plasma was assayed for HIVAg using a solid phase immunoassay employing beads coated with human anti-HIV (Abbott Laboratories, North Chicago, IL U.S.A.). Of the 83 seropositive men, including the 23 who seroconverted, 34(42%) had HIVAg. The occurence of HIVAg was associated with a decline in concentrations of antibody to p24 as determined by intensity of precipitation bands seen on immunoblots. 32(39%) developed HIVAg when relatively symptom-free and within 2-22 months after entry, 22(26%) developed AIDS. 2(2.4%) subjects were HIVAg positive after diagnosis of AIDS. Only 3 participants progressing to AIDS did not demonstrate HIVAg. HIVAg was not detected before antibody developed in men with incident infection. Mean interval between the first detection of HIVAg and diagnosis of AIDS was 315 days (range 56 to 688) in the 22 men with prior HIVAg (Gp1). Mean CD4 number at the first time of detection of HIVAg before the diagnosis of AIDS was 311 cells/mm^3 $\pm$ 164 (s.d.). Mean CD4 counts in the 10 men with HIVAg who did not develop AIDS (Gp 2) was 481 cells/mm^3 $\pm$ 202 (p=0.03 vs Gp 1), and in seropositive men without HIVAg (Gp 3) 710 cells/mm^3 $\pm$ 345 ($p < 0.0001$ vs Gp 1; $p = 0.01$ vs Gp 2). The most common clinical finding in HIVAg positive men was generalized lymphadenopathy (56%), although 35% of participants were asymptomatic and 26% had AIDS-related symptoms at the time HIVAg was detected. HIVAg commonly predates the onset of the opportunistic diseases which define AIDS and is associated with severe CD4 depletion.

Virology—Antivirals

T.4.1 Activity of 2',3'-Dideoxynucleosides as Single Agents or in Combinations against Pathogenic Human T-Lymphotropic Viruses In Vitro.
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Purines and pyrimidines with the ribose moiety in a 2',3'-dideoxy-configuration can significantly inhibit the in vitro replication of a wide range of retroviruses without inhibitions of the growth and functions of target cells. Dideoxynucleoside analogues including erythro-3'-azido-2',3'-dideoxythymidine (AZT) can completely block the infectivity and cytopathic effect of HTLV-III (also called LAV or HIV) against T-cells under conditions of the substantial virus excess. Dideoxynucleoside analogues also block the in vitro infectivity of HTLV-I, which can cause a wide spectrum of diseases including adult T-cell leukemia, immunodeficiency state, and neurological abnormalities. A variety of dideoxynucleoside derivatives have been tested for the activity against HTLV-III. For example, the antiviral activity of 5-fluoro-2',3'-dideoxycytidine is as potent as its parent analogue, dideoxycytidine (ddC), while 5-bromo-, or 5-methyl-ddC is inert against the virus. In cells protected by dideoxynucleoside analogues the viral DNA synthesis and viral mRNA expression can not be detected. Dideoxynucleoside-5'-triphosphates strongly inhibit HTLV-III reverse transcriptase (RT) activity but much less mammalian DNA polymerase alpha activity. These 5'-triphosphates serve as substrates for the HTLV-III RT to elongate a DNA chain by one residue, after which the chain is terminated. In the case of ddC, the relative intracellular concentrations achieved in vitro exceed those needed for the DNA-chain termination. Combination of AZT and acyclovir shows a synergistic antiviral effect in vitro. Combination of AZT and dideoxyadenosine or ddC also shows a significant antiviral effect at low concentrations. These studies may provide leads in current attempts to develop regimens for effective chemotherapy against pathogenic human retroviruses.

T.4.2 Inhibitory Effect of Various Reverse Transcriptase Inhibitors on Tumor Induction by Moloney Murine Sarcoma Virus in vivo
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Tumor induction by Moloney murine sarcoma virus (MSV) in newborn NMRI mice is a representative model for retrovirus infection in vivo. Daily treatment with 3'-azido-2',3'-dideoxythymidine (AzddThd) (125 mg/kg/day) protected more than 80 % of the MSV-infected mice against tumor formation and more than 90 % against death. Even treatment with 25 mg/kg/day of AZT significantly delayed tumor formation, prolonged the life span, and protected 30 % of the infected mice against death. In contrast, treatment with either 125 mg/kg/day of 2',3'-dideoxycytidine (ddCyd) or 625 mg/kg/day of 2',3'-dideoxythymidinene (ddeThd) only resulted in a slight delay of tumor formation and no increase of survival rate. Mice treated with ddCyd at 625 mg/kg/day developed symptoms of acute toxicity, such as anemia, resulting in death within 10 days after the beginning of treatment. Combination treatment of ddCyd with deoxythymidine prolonged the life span and protected several of the infected mice against death. 2',3'-Dideoxythymidine (ddThd) did not protect mice against tumor formation and death, even at a dosage of 625 mg/kg/day. Other reverse transcriptase inhibitors, i.e. suramin, Evans Blue and aurintricarboxylic acid, were also ineffective in protecting the mice against tumor formation and death at nontoxic doses.

T.4.3 Anti-HIV Properties of Castanospermine.
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Castanospermine (CAS, 1,6,7,8, tetrahydroxyoctahydroindolizine) is a plant alkaloid that has been shown to be a potent inhibitor of glucosidase I, and thereby prevents normal processing of glycoproteins. We tested whether this compound might inhibit the function of the HIV envelope in infection and cytopathicity. CAS dramatically inhibited syncytium formation in a transfected CD4+ cell line expressing the HIV env gene. CAS effects on HIV replication were also examined using freshly HIV infected H9 cells treated with CAS. A dose-dependent protective effect was observed, as assayed by cytopathic effect, reverse transcriptase activity, p24 radioimmunoassay, radioimmunoprecipitation, and virus yield. The effect was greatest at doses which did not significantly alter cell viability. CAS appears to exert its antiviral effects by alteration of the env glycoprotein and not by alteration of the CD4 molecule. T4-gp120 binding is not altered by CAS, but processing from gp160 to gp120 is decreased by this compound, suggesting that this is the mechanism of inhibition of syncytium formation. Antiviral effects of CAS appear to result from a decreased virion infectivity due to inference with post-T4-binding steps in virus entry, as well as a decrease in cell-to-cell virus transmission secondary to syncytium inhibition. Experiments evaluating possible synergistic effects of CAS with other anti-HIV agents are currently underway.

T.4.4 Phosphorothioate Analogs of Oligodeoxynucleotides: Novel Inhibitors of Replication and Cytopathic Effects of HTLV-III/LAV(Human Immunodeficiency Virus) in vitro
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Nuclease-resistant phosphorothioate analogs of several oligodeoxynucleotides were tested in vitro for antiviral activity against HTLV-III/LAV on human T-cells. Two anti-sense sequences (14-mers) complementary to the HTLV-III/LAV genome, a sense sequence, a random sequence, and homo-oligomers of dA and dC of two lengths (14 and 28-mers) exhibited a significant inhibitory effect on viral replication and cytopathogenicity under conditions of viral excess. The antiviral activity was strikingly linear with GC content; longer phosphorothioate analogs were more effective than shorter ones. None of the homologous sequences of unmodified normal oligomers, methylphosphonate analog, nor the 3-methylthymine containing phosphorothioate analog (the latter would be chemically blocked from binding to complementary sequences) showed any antiviral effects. The de novo synthesis of viral DNA was completely inhibited by 28-mer dC phosphorothioate at $\geq$ 1μM as assessed by Southern blot hybridization. However, even 25μM of 28-mer dC phosphorothioate showed no significant inhibitory effect on the expression of p24 gag protein in chronically infected cells. These results suggest that the antiviral effect of phosphorothioate analogs of oligodeoxynucleotides is brought about by binding to certain viral component(s), possibly viral nucleotide sequences and thereby inhibiting de novo synthesis of viral DNA. We have also observed that 14-mer dC phosphorothioate synergistically enhanced the antiviral effect of 2', 3'-dideoxyadenosine. These data suggest that phosphorothioate analogs of oligodeoxynucleotide could be a novel class of therapeutic agent against acquired immunodeficiency syndrome (AIDS) and related diseases.

T.4.5 Tumor Necrosis Factor-α and Interferon-γ Have Anti-HIV Activity
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One consequence of the defective immune response in patients with acquired immunodeficiency syndrome (AIDS) is an impaired synthesis of cytokines. The cytokines tumor necrosis factor-α (TNF-α) and interferon-γ (IFN-γ) act synergistically to protect cells against HIV infection in vitro. In the presence of the two cytokines, expression of the viral antigen p24 and HIV RNA is dramatically reduced while levels of reverse transcriptase activity and production of infectious HIV particles are strongly inhibited. Combinations of TNF-α and IFN-γ kill cells acutely infected with HIV and inhibit the production of full length genomic size of HIV mRNA in chronically infected H9 or HuT-78 cells. HIV infection does not induce the production of TNF-α or TNF-β mRNA, but HIV-infected cells are able to produce TNF mRNA in response to mitogens.

T.4.6 QUANTITATION OF THE HUMAN IMMUNODEFICIENCY VIRUS IN PATIENTS TREATED WITH ANTIVIRAL AGENTS
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Identification of HIV-infected cells and determination of virus titers directly in individual's blood (i.e. prior to virus amplification) are critical factors in the prognosis and possible therapeutic interventions of patients at risk to develop AIDS. We have developed an extremely sensitive in situ hybridization method using molecularly cloned HIV-probe to quantitate the number of HIV infected cells prior to culturing in vitro. A combination of this method with short-term culturing and antigen detection assay, offers one of the most sensitive and specific systems to detect and to quantitate levels of viral RNA, reverse transcriptase, proteins as well as cytopathogenicity of HIV in patients at risk to develop AIDS. These techniques are particularly useful for comparison of the results before and after the treatment of patients with the drug. Furthermore, antiviral effects of various chemical compounds that are currently being used for clinical trials in HIV-infected individuals can be quantitatively assessed at the level of specific cell types that may be involved in the pathogenesis of AIDS.

Clinical Management—Neurology

T.5.1 The Brief Neuropsychological Examination for AIDS Dementia Complex: Correlations with Functional Status Scales and Other Neuropsychological Tests

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The AIDS dementia complex (ADC) is a progressive syndrome that is a frequent complication of HIV infection. Although the natural history of ADC has not been fully characterized, experience with moderate and severe ADC has suggested that it shares features with the "subcortical" dementias. In order to better characterize the natural history of ADC as well as systematically assess the effects of antiviral therapies in multi-center studies, we have developed a brief battery of neuropsychological tests that are sensitive to some of the major features of ADC: motor slowing, poor concentration and reduced spontaneity. The tests include verbal fluency, Trail Making A, Trail Making B, digit-symbol substitution, finger tapping with dominant and non-dominant hands, and a timed gait test. Our initial experience with these tests indicates significant decrements in performance across patient groups with increasing severity of HIV infection ranging from asymptomatic HIV infection to AIDS. Moreover, in a series of 100 evaluations in over 60 AIDS patients, these tests correlated significantly with a number of function status scales including Karnofsky, Kurtzke and Blessed Scales, and, more importantly, with AIDS-specific neurological history and examination scales (correlations ranging from r = .4 to r = .8), and other neuropsychological tests including additional WAIS subtests, memory and motor tests (correlations ranging from r = .4 to r = .9). This brief battery constitutes a functionally significant core of tests that is suitable for inclusion in large population natural history and therapy studies.

T.5.2 Neurologic and Neuropsychologic Complications of Lymphadenopathy Syndrome.

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To determine whether there is an association between neurologic and neuropsychologic abnormalities and human immunodeficiency virus (HIV) infection in lymphadenopathy syndrome (LAS), we studied 39 seropositive patients with unexplained lymphadenopathy for >3 months (mean duration of LAS=4.1 years) and 38 homosexual/bisexual men (controls) who were seronegative for HIV. Participants were evaluated with a neurologic symptom questionnaire, neurologic examination, a 5-hour battery of neuropsychologic tests, immunologic tests, and magnetic resonance imaging. Fifteen patients (38%) with LAS had histories of symptoms of peripheral neuropathy and 9 (23%) had a history of herpes zoster radiculitis. Overall, 21/39 (54%) patients and 3/38 (8%) controls had a history of symptoms or signs of neurologic abnormality (odds ratio=13.6; $p<0.001$). By neuropsychologic assessment, 9/18 (50%) patients and 2/26 (8%) controls were abnormal (odds ratio=12.0;$p<0.002$). Of those abnormal on the neuropsychologic assessment, the majority scored in the mildly impaired range. Magnetic resonance imaging was abnormal in one patient and one control. Neither neurologic nor neuropsychologic abnormalities correlated with absolute T-helper lymphocyte count or T-helper/T-suppressor lymphocyte ratio. These results indicate an association of neurologic and neuropsychologic abnormalities with LAS. They suggest that mild neurologic abnormalities in LAS are common and that HIV may be the cause.

T.5.3 Cerebrospinal Fluid(CSF) Findings in HIV-infected Persons Without Clinically Evident Neurologic Disease

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To evaluate the frequency of subclinical CNS infection with HIV, we performed cerebrospinal fluid(CSF) examinations and CSF cultures for HIV on 24 homosexual men with AIDS(post PCP without other active infections, mean age 36) and 10 subjects with persistent generalized lymphadenopathy(PGL, mean age 37). None of the 34 subjects had clinical symptoms or signs of CNS dysfunction. All AIDS patients had Karnofsky scores ≥ 70 and all PGLs had scores ≥ 80. Mean T4 counts were $100/mm^3$ and $560/mm^3$ in the 2 groups; all AIDS and 3 PGLs had T4 counts $<400/mm^3$. All were HIV-seropositive. HIV was isolated from peripheral blood lymphocytes in all 34 patients. HIV was isolated from unfiltered CSF in 42% of AIDS and 50% of PGL subjects. CSF pleocytosis(>5 WBC/mm^3) was noted in only 3 of the HIV+ CSFs; 6 had CSF protein >40mg/dl. All CSFs had normal glucose values; none had detectable cryptococcal antigen or other viral pathogens. There were no differences in any CSF, clinical, or immunologic parameters in CSF HIV-positive and negative subjects. HIV can be isolated in CSF from half of AIDS and PGL patients without constitutional complaints or overt neurologic symptoms or signs. The frequency of CSF HIV infection appears unrelated to the clinical stage of disease. The clinical significance of CSF HIV is unknown at present and requires further study.

T.5.4 Cerebrospinal Fluid (CSF) Study in Forty-Four HIV-Infected patients: Clinical Correlation with Virus Isolation and Intrathecal Specific Antibodies Synthesis.

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CSF of 44 patients - 24 AIDS, 15 ARC, 5 asymptomatic - were studied for presence of HIV in culture and antibodies by Elisa. None had neurologic opportunistic infections. Intrathecal HIV-IgG synthesis (Σ Ab) was assessed on a ratio CSF-HIV x serum Alb : serum HIV x CSF alb ≥ 2. Presence of HIV was demonstrated by detection of reverse transcriptase activity in supernatant of cultures during 7 weeks. CSF characteristics and computerized tomography were recorded. 28/44 patients (57%) had neurologic disorders possibly related to HIV : encephalopathy (18), polyneuritis (3), meningitis (3) myelopathy (1), and 19 were asymtomatic.

	V ⊕ ΣAb ⊕	V ⊕ ΣAb ⊖	V ⊖ ΣAb ⊕	V ⊖ ΣAb ⊖	TOTAL
-Number of patients	13	5	22	4	44
-with possibly HIV neurologic disorders	8/13	5/5	12/22	0/4	25

Prevalence of HIV infection was high (91%) attested either by isolation of virus (41%) or specific antibodies intrathecal synthesis (50%). But this was not significantly associated with clinical evidence of HIV-nervous system involvement since 28% (5/18) of the patients with positive CSF culture and 45% (10/22) of those with intrathecal antibodies synthesis were neurologically asymptomatic.

These results suggest that the clinical signification of the presence of HIV in CSF remains unclear.

T.5.5 The Clinical Spectrum and Time Course of HIV-associated "Aseptic" Meningitis

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To better define the entity of HIV-associated meningitis, we reviewed the results of 80 consecutive diagnostic lumbar punctures in homosexual men with HIV infection to identify those with CSF pleocytosis. Twenty individuals had ≥ 6 cells per mm^3. Six of these had a secondary opportunistic infection documented. Fourteen others had no secondary pathogen or neoplasm identified by CSF cultures or cerebral imaging studies. All 14 were either known to be HIV seropositive at the time of study or had prior manifestations of HIV disease, including 3 subjects with KS. None of the 14 had prior major opportunistic infections. Two patterns of disease were observed. Six men (group 1) had acute onset of a self-limited illness characterized by headaches and fever, with meningeal findings in 3. One of 6 had a focal neurological deficit. Eight (group 2) had a more indolent course. Seven had chronic headaches, no fever and no meningeal or neurological findings. One presented with cognitive dysfunction and ataxia but no headache. Mean values of CSF leukocytes and protein were higher in group 1 patients. Pleocytosis lasted for several months in 2 patients in group 2 who were restudied. CSF HIV culture was positive in 3 of 4 cases studied. We conclude that HIV-associated meningitis occurs commonly and relatively early in the course of HIV infection compared to HIV encephalopathy. Headache rather than cognitive dysfunction is the most common clinical manifestation. The course can range from an acute meningitis to more low grade chronic symptomatology. CSF inflammation usually differentiates this condition from other HIV-associated neurological complication. HIV-associated meningitis does not necessarily predict the development of other HIV-related neurological syndromes.

T.5.6 Polyneuropathies in Subjects Infected with HIV

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The neurotrophic effects of HIV are well documented. It can be directly or indirectly responsible for a wide variety of peripheral disorders and symptoms. In order to detect clinical and infraclinical polyneuropathy we undertook a prospective study on the peripheral nervous system of HIV seropositive subjects (38 men and 2 women) with a mean age of 31 years (range 20 - 24). This population included 22 homosexuals, 13 drug addicts, 1 addicted homosexual and 4 bisexuals. Five were symptomless carriers, 13 had ARC and 22 had AIDS. All 40 patients underwent clinical neurological and electrophysical (E.M.G., motor conduction and sensitivity, F waves) examinations and sural nerve biopsy was performed on 23/40 (57,5 %).

Peripheral neurologic anomalies, mainly quadridistal paresthesia, were noted in 18/40 patients (45 %). In 27/40 patients (67,5 %) clinical examination revealed evidence of sensory neuropathy : especially distal hypoesthesia to touch and vibration and, less often, hypoesthesia to pin pricking and loss of Achilles jerk. Electrophysiologic data was more or less corroborative of exclusively or predominantly sensory polyneuropathy 33/40 patients (82,5 %) : midly lowered sensory motor conduction or greatly lowered action potentials and less often spontaneous denervation or prolongation of F wave latency. The results of 14/23 nerve biopsies are available. In 10/14 findings showed neuropathology involving axons (8 cases), myeline sheath (1), and circulatory impairment (1). Sensory polyneuropathy is frequent in subjects infected by HIV and especially in AIDS patients. It is usually well-tolerated with mild and even no symptoms and slowly degenerative.

TUESDAY, JUNE 2

Prevention/Public Health—Reaching the General Public

T.6.1 Market Research for Australia's National AIDS Education Program
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The Program's objectives are: (a) to provide factual information to the total population and (b) to motivate individuals to adopt behaviors to reduce viral transmission.

To identify areas of need, preparatory market research was undertaken. This included: (a) a 30-minute interview/questionnaire covering 750 men and 750 women aged 16 to 60 from the general population; (b) 30-minute questionnaires administered to 200 children aged 12-15 years; and (c) surveys of gay men and IV drug users involving detailed interviews and questionnaires.

Preliminary results for adults showed public awareness that casual transmission is not likely (76%), that condoms can reduce the risk of transmission (93%), and that vaccines are not available (94%). However only 19% were correct on 7 of 8 knowledge items, condom usage appears to be low and 40% still consider the blood supply unsafe. Only 49% are aware of heterosexual transmission and 36% of needle sharing as transmission routes. Seventy-two per cent disagree that sex should be limited to marriage. The public approved general population (91%), childhood (81%) and risk group (80%) educational programs. Barriers to education include lack of perceived immediacy of threat (50%) and the belief that one's own knowledge about AIDS is adequate.

T.6.2 Evaluation of Health Education in Britain.

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In the United Kingdom today the Government has embarked upon Health Education and have utilised National Press, Television advertisements and Household leaflet drops. This study presents data on the evaluations of these steps.

Higher and lower risk subjects, comprising consecutive attenders at STD clinics, General Practice clinics and university students were monitored before and after each campaign. It wes shown that maximum impact occurs at the first time a medium was used (41.9% overall noticing advertisements at first down to 24.1%). Quality of content was initially low and improved as attention decreased. Prior to the press campaigns knowledge was limited and errors and anxiety were high. The press campaign increased levels of information (t=2.13 df 516 p=.03 (first campaign) t=3.97 df=417 p=.001 (second). Closer analysis showed that this was accounted for by filling in gaps and not adjusting misconceptions. The campaigns had no effect on changing sexual behaviour.

Television advertisements had minimal information and used fear arousal to draw attention to leaflets. Exposure was high (95% of subjects monitored had seen the advertisement). General and health education value were low. Subjects found the household leaflet useful. Subjects still state the medical profession as their desired primary source for information.

T.6.3 What the Public Wants to Know: The National AIDS Hotline

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In mid-December 1986, operation of the national hotline for AIDS information was transferred from the Centers for Disease Control to the American Social Health Association. The hotline provides a taped message which refers callers to an operator for further information. The new service was expanded from 5 days/week, 9 hours/day to 7 days/week, 24 hours/day coverage. In the first month of operation, the number of calls steadily increased, with taped messages going from 600/day to 1,700/day at its peak and operator calls from 100/day to 700/day. Twenty-six percent of the operator-answered calls were received on weekends or holidays; 30% were received between the hours of 6 pm and 8 am.

Based on a sample of every fifth operator call, most were to request information (89%), with highest demand for information on means of transmission (33%), general information (27%), or testing (15%). The average call lasted 6.8 minutes. Most calls were made because the caller was curious (51%), though a high proportion requested information because they had either symptoms of AIDS, had been tested positive, or had a test pending (23.7%). Most callers were male (52%); 12% of men and 1% of women callers identified themselves as gay. Information was requested by 16% of callers, with twice as many requests coming from women as from men, and the highest proportion of mailings was to the northeast (30%).

T.6.4 THE EFFECT OF A GOVERNMENT AIDS MEDIA CAMPAIGN ON A GENERAL POPULATION : ANTIBODY TEST REQUESTS AND REASONS.
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The impact of a Government television, newspaper and billboard AIDS advertising campaign was assessed by comparing the numbers of requests for antibody testing in the three months before and after the campaign began. Numbers were compared in five groups : homosexual and heterosexual men, bisexual men, heterosexual women and bisexual women. Reasons given for requesting the test were also compared.

In the three months after the campaign, the numbers overall increased by 239%. Across groups, the numbers were as follows:

	Hom. Men	Het. Men	Bi. Men	Het. Women	Bi. Women	N
Pre:	58.7%	20.2%	8.4%	12.4%	0.3%	431
Post:	27.8%	37.4%	7.7%	26.8%	0.3%	1032

While the actual number of homosexual men and bisexual women requesting the test remained constant, the numbers of heterosexual men and women wanting the test increased four and five-fold respectively. The number of bisexual men doubled. In lower-risk groups, requests for testing concerned anxiety over casual sexual contacts at home and abroad. No-one from these groups was found HIV antibody positive, and 8% (n=16) were found seropositive from homosexual and bisexual male attenders. The Government campaign appears to have raised considerable anxieties in the lowest-risk groups while having little impact in groups with known higher seroprevalence

T.6.5 Evaluation of School-Based AIDS Education Curricula in San Francisco

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To design and develop effective AIDS prevention curricula for middle school and high school students in San Francisco, we conducted a baseline survey, teacher trainings, and evaluation of a pilot demonstration program. The baseline survey showed insufficient knowledge of HIV prevention and misconceptions about casual contagion. We subsequently developed AIDS curricula and piloted them in 3 middle schools and 3 high schools. Non-intervention control classes were surveyed at each of the middle and high schools. All 640 students completed a pretest. The intervention group received 3 periods of AIDS instruction. A post-test, identical to the pretest, was administered to both groups. Pretests showed that both had comparable knowledge. Post-tests indicated that students in the intervention group had a significantly higher mean score for AIDS knowledge ($p<0.0001$) than the control group. Specifically, 88% of the students in the intervention group were aware that condoms are one way of preventing AIDS compared to 71% in the control group ($p<0.0001$), and 90% in the intervention group agreed that is is unsafe to have sex with someone whose health history is unknown compared to 81% of the control group ($p<0.0001$). We conclude that specially designed AIDS curricula can significantly increase adolescents' short-term knowledge which may result in changes to lower-risk sexual behavior.

T.6.6 AIDS and Adolescents: Knowledge, Beliefs, Attitudes and Behaviors
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Adolescents are a group at high risk for exposure to AIDS. A random sample survey of 860 16-19 year olds in Massachusetts indicates that many adolescents are still misinformed or confused about AIDS and AIDS transmission. Fifty-five per cent of the adolescent respondents said they are sexually active but only 15 per cent of them reported changing their sexual behavior because of concern about contracting AIDS, and only 20 per cent of those who changed their behavior used effective methods. Eight per cent of both sexually active and inactive adolescents did not know that AIDS is transmitted by heterosexual sexual intercourse. Thirteen per cent had used psychoactive drugs other than alcohol and marijuana with one per cent injecting drugs. Of those psychoactive drug users 8 per cent did not know that AIDS can be transmitted by injecting drugs. There is no significant difference in knowledge between the sexually active and non-active adolescents concerning sexual behavior and AIDS transmission, or between the drug users and non-users concerning drug use and AIDS transmission. Because their knowledge of the mode of AIDS transmission is limited many adolescents, including those in the highest risk subgroups of sexually active or psychoactive drug users, do not know what sexual and drug precautions are needed to prevent transmission of the virus. School systems and health care providers should systematically educate this population about AIDS to counter the current misinformation and confusion.

Epidemiology—Surveillance: Incidence, Prevalence and Trends

T.7.1 Temporal Trends of Prevalence and Incidence of HIV Infection Among Civilian Applicants for US Military Service: Analysis of 18 Months of Serological Screening Data.

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Each month since October 1985, approximately 50,000 civilian applicants for U.S. military service have been screened for antibody to HIV. Of the 641,917 applicants screened during the program's first 12 months 86% were male, 74% were white (not hispanic), and 57% were younger than 21 years. Applicants represented all 50 states, the District of Columbia, and several U.S. territories. Overall (1.5/1000), sex-specific (male: 1.6/1000, female: 0.6/1000), and age-specific prevalences did not significantly vary between the first six-months of screening and the second. A "temporal trend term" (first six month period vs. second six-month period) did not predict antibody status in a multivariate model that controlled for birth year, race/ethnicity, sex, population density, and regional AIDS incidence. When data from high antibody prevalence sub-groups were analyzed separately, there were suggestions of an independent effect of a "temporal trend term." For example, among black male applicants, the adjusted odds ratio (second six months vs. first six months) was 1.07 (95% CI: 0.97-1.18). Estimates of prevalences, incidences, and temporal trends, overall and in demographically and geographically defined sub-groups, from 18 months of screening data will be presented.

T.7.2 Analysis of Demographic and Epidemiologic Data Concerning HIV Antibody Positive Recruits and Active Duty Air Force Members.

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Since the beginning of testing for HIV antibody by the U.S. Air Force, over 268 active duty members (ADM) and 38 recruits (REC) have been identified as being positive using both an Elisa and Western Blot techniques. The majority of both groups are asymptomatic; AIDS has been diagnosed in 14.9% of ADM. The overall incidence of seropositivity has remained relatively constant at approximately 0.1% (one per thousand) for REC and ADM. REC and ADM have all been interviewed for demographic variables and examined by the infectious disease service. The average age for REC was 21.8 and for ADM 26.9. The percentage of males was 97% REC/96% ADM. A racial difference was observed between REC and ADM with proportionately more black than white REC positive for HIV. Referral locations were diverse and reflected US Air Force assignments in general. Only 19% REC/11.5% ADM admitted to homosexual or bisexual activity. The mean number of heterosexual partners of REC/ADM was 13.8/68.4 with a range from 1 to > 1000 lifetime partners. Homosexual partners were more frequent: mean > 200. Marriage was infrequent, as predicted, in REC. Twenty nine percent of ADM were married. Age at first intercourse was similar in both groups. Among heterosexual REC and ADM, despite lower sexual promiscuity than occurs in homosexual populations, sexually transmitted diseases were frequently reported. REC/ADM gonorrhea occurred in 30/37%, syphilis in 11/11.5%, herpes simplex 3/6%. NGU and condyloma acuminata were reported more frequently in ADM, 17.3% and 13.5% respectively. Exposures to prostitutes ranged globally from Europe to Southeast Asia and was highly reported in ADM, 37%. Although heterosexual preference in sexual activity and exposure to prostitutes suggests a higher transmission rate by heterosexual sex in the Air Force, disproportionate prevalence of anal condyloma in ADM not admitting to association with high risk groups suggests non-truthful reporting of sexual preference by some ADM and REC.

T.7.3 AIDS in Heterosexual Contacts: a Small but Increasing Group of Cases

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Patients with AIDS who have no identified risk other than heterosexual contact represent 4% of all AIDS patients reported in the United States. As of January 16, 1987, this group includes 521 patients who had heterosexual contact with a person with AIDS or at risk for AIDS (HC) and 589 persons who were born in foreign countries where heterosexual transmission plays a major role. The racial/ethnic distribution of the 521 HC patients is similar to that associated with IV drug abuse: 48% black, 26% Hispanic, 25% white, and 1% Asian. Males account for only 18% of HC cases versus 78% of non-HC patients who are heterosexual in orientation. The proportion of male HC patients has not increased significantly since 1983. The geographic distribution of HC patients differs significantly by sex: 67% of females are reported from New York, New Jersey, and Florida, compared with 43% of males ($p<0.0001$). The "at-risk" sexual partners of the HC patients include IV drug abusers (64%), bisexual males (female HC patients only) (14%), individuals from countries where heterosexual transmission plays a major role (4%), transfusion recipients (1%), and hemophiliacs (1%). Risk status of the contact partner is under investigation for the remaining 16%. During 1986, the total number of reported HC patients increased by 135% from 218 to 513, while reported cases among homosexual/bisexual men and IV drug abusers increased by 82% and 81% respectively. This reflects a 10 month doubling time for HC cases compared with a doubling in 14 months for homosexual/bisexual men and IV drug abusers. HC patients have increased from 1.0% of all AIDS cases in 1983 to 2.3% in 1986 ($p<0.0001$). Although the overall proportion of HC cases remains small, it will increase. Additional studies are needed to characterize and track this group.

T.7.4 Incidence of HIV Infection in Homosexual Men in a High Risk Area: Implications for Vaccine Trial Design.

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Early in 1984 the Laboratories of Epidemiology and Immunogenetics of The New York Blood Center enrolled a cohort of 850 homosexually active men in a prospective study of the acquired immune deficiency syndrome. Of the 773 men tested for anti-HIV by ELISA (Dupont) and Western Blot (Biotech) at entry, 57.7% were seronegative and therefore were considered susceptible to HIV.

In the three years since the study began, the participants returned for follow-up every 4 months. As risk factors related to HIV infection became known, the men were periodically advised regarding unsafe sexual practices. As a consequence, sexual activity changed dramatically, especially in numbers of partners and frequency of receptive rectal intercourse. However, in these past 3 years 37 men have seroconverted, a life-table attack rate of 10.0%. The 4-month incidence decreased from 2.25% in the first 4 months to 0.68% by the fourth interval at 1-1/2 years. Since then, however, the incidence has remained stable at about 1% in each 4-month interval. Seroconversion highly correlated, but not exclusively, with the practice of receptive rectal intercourse and nearly 35% of seronegative men continued this practice despite advice to the contrary. These data suggest that, despite educational efforts regarding safer sex, some homosexual men persistently engage in high risk sex. Such men may be candidates for vaccine efficacy trials if vaccines become available for testing. Additionally, the appearance of multiple antibodies to HIV proteins and T-lymphocyte alterations at the time of seroconversion suggest end-points which may distinguish between vaccine and virus-induced antibody and end-points for evaluation of vaccine efficacy.

T.7.5 The Surveillance of Clinical Viral Hepatitis Type B and Primary, Secondary and Early Latent Syphilis in Homosexual and Bisexual Men in MN: Implications for Human Immunodeficiency Virus (HIV) Transmission

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Since 1982, a marked decline in the incidence of rectal gonorrhea and syphilis has been noted among homosexual men nationwide. To determine the implications of declining rates of selected bacterial sexually transmitted diseases (BSTD's) on HIV transmission among homosexual and bisexual men, we compared statewide surveillance data for these groups obtained between January 1982 and July 1986 for incident cases of primary, secondary and early latent syphilis and acute clinical viral hepatitis type B (with hepatitis B serving as a marker for the sexual transmission of HIV). A mean of 79 cases (range, 61 to 90) of syphilis occurred during each six-month interval before July 1984. Despite similar surveillance efforts, marked decrease in incident cases was noted between July 1984 and June 1986, with a mean of 16 cases (range, 11 to 21) reported for each six-month interval. However, no change was noted in the number of acute clinical hepatitis B cases reported through active laboratory-based surveillance. The number of clinical hepatitis B cases reported by six-month interval ranged from 12 (July-December 1983) to 19 (January-June 1986); intravenous drug abuse could be documented as a risk factor for only 8% of cases. Results of this study indicate that among homosexual and bisexual men declining rates of syphilis and other BSTD's among homosexual and bisexual men may not reflect a concurrent reduction in the transmission of selected viral STD's, such as viral hepatitis type B. We believe these results may have significant implications when interpreting the impact of risk reduction programs on HIV transmission nationally.

T.7.6 Community Surveillance for HIV Infection in Zaire

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To assist Zairian physicians in diagnosing HIV infection, a no-cost screening program was established at Mama Yemo Hospital, Kinshasa. Despite logistic difficulties in transport, sera from 8871 patients were referred during 1986, of which 54% was HIV(+) by repeat ELISA. Among children 70% of cases occurred between the age of 0-3. Three times as many children aged less than 1 year were HIV(+) compared to children aged 1-3 years old. Seventy percent of all cases occurred in patients aged 15-40 years. Striking differences in the female: male sex ratio were observed: less than 15 years old F:M ratio=1:1; 15-30 years F:M ratio=6:1; greater than 30 years F:M ratio=.64:1.

The diagnostic accuracy(number of tests positive/total tests submitted) of physicians working in the Tuberculosis Sanitorium or in adult diarrheal disease wards were the highest; 85% and 74%, respectively. These data document in Zairian physicians a considerable awareness of and ability to clinically diagnose HIV infection.

The overall female:male infection ratio in our study(1.1:1) is similar to the figure widely used in describing the epidemiology of HIV infection in Africa. However, we found that cases of infection clustered in two risk groups, young women(age 13 to 25) and middle to older aged men. These differences in age-specific, sex-specific HIV infection rates should be considered before any HIV prevention activities involving behaviorial modification in Africa are initiated.

Clinical Trials—AZT and Ribavirin

T.8.1 Decline in Serum HIV p24 Antigen (Ag) in Patients Treated with AZT.

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To assess the anti-retroviral effect of AZT in vivo, we measured serum HIV-Ag in 157 AIDS or ARC patients enrolled in a multicenter placebo-controlled trial. Patients received AZT 250 mg or placebo every 4 hrs, with dose reduction for toxicity. HIV p24 Ag was detected using a polyclonal IgG sandwich enzyme immunoassay. Sera were obtained at entry and at 4 week intervals. 36 of 79 (46%) AZT patients and 40 of 78 (51%) of placebo patients had Ag detected during the trial. 28 patients in each group had a baseline and later specimen for comparison. Baseline HIV-Ag levels were 297 pg/ml for AZT patients and 234 pg/ml for placebo patients (p=NS).

Significant decreases in HIV-Ag in AZT patients were seen at 4 weeks (AZT group mean = 70 pg/ml, placebo mean = 223; p=0.0002), 8 weeks (AZT mean = 56 pg/ml, placebo mean =283, p< 0.0001) and 12 weeks (AZT mean = 53 pg/ml, placebo mean 84 pg/ml; p=0.0052). Differences persisted through 20 weeks, though sample sizes were small. No HIV-Ag positive subject in either group had anti-p24 antibodies, and decline in HIV-Ag in AZT patients was not associated with reappearance of anti-p24. We conclude that HIV-Ag levels are an important marker of anti-retroviral activity in a substantial proportion of AIDS and ARC patients.

T.8.2 Therapy of AIDS Patients with Early Kaposi's Sarcoma with 3'-Azido-3'Deoxythymidine

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3'-Azido-3'-deoxythymidine (AZT) is a nucleoside analogue which has been shown capable of inhibiting the replication of HIV in vitro and prolonging life in AIDS patients 120 days following an initial bout of Pneumocystis carinii pneumonia. The present study was designed to determine the effects of AZT on a group of patients at an earlier stage of HIV infection, namely AIDS patients with Kaposi's sarcoma only and with more than 200 T4 lymphocytes/mm^3. A 40 patient study was designed with patients randomized to 1 of 4 groups. Group 1 patients received placebo, group 2 patients received 250 mg AZT po q4h, group 3 patients received 0.05 mg/kg AZT iv q4h, and group 4 patients received 2.5 mg/kg AZT iv q4h. Patients were treated for 12 weeks. As of this writing, 36 patients have entered the study and 22 have completed 12 weeks. Analysis of the available data has revealed that there was a reduction in Kaposi's sarcoma in 0/6 patients on placebo and 4/16 patients on drug. Viral cultures have become negative in 1/6 patients on placebo and 6/15 patients on drug. No significant changes have been seen in immunologic parameters including total lymphocyte and subset counts, lymphocyte blast transformation to mitogens or antigens or natural cytotoxicity. Thus, based upon reduction in KS lesions and decline in viral shedding, AZT may be of value for the treatment of early AIDS patients with Kaposi's sarcoma.

T.8.3 Clinical Evaluation of the Central Nervous System in HIV Infected Patients on Azidothymidine (AZT).

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During a double-blind, placebo-controlled trial of AZT, 32 AIDS and ARC patients in San Diego were intensively investigated to detect any effect of AZT on the central nervous system. In addition to the standard protocol, study participants had: peripheral blood and CSF culture to detect HIV; magnetic resonance imaging (MRI) of the brain; a detailed clinical neurological examination; and a comprehensive neuropsychiatric assessment. There was no effect of AZT on the frequency of positive HIV culture in blood or CSF, nor on the patterns of MRI abnormality. The clinical neurological examinations showed a beneficial effect of AZT; 0/13 patients improved in the placebo group, and 5/16 in the treated group. However, the overall effect did not meet criteria for statistical significance (P = 0.12, Mantel-Haenzel Test). Neuropsychiatric testing detected no difference between the groups. These studies have been extended in two ways. First, CSF specimens are under analysis to determine HIV antigen load, using an antigen capture assay. Second, the clinical neurological examination data is being pooled with comparable data in a further 30 patients from another AZT study center (Miami) to evaluate better the significance of the differences described here. Our working hypotheses are: (1) that AZT leads to an improvement in neurological functioning, and (2) that physical neurological examination is the most sensitive available technique to detect this effect.

T.8.4 THE TOXICITY OF 3'-AZIDO-3'-DEOXYTHYMIDINE (AZIDOTHYMIDINE) IN THE TREATMENT OF PATIENTS WITH AIDS AND AIDS-RELATED COMPLEX: A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

AZT COLLABORATIVE WORKING GROUP

A double-blind, placebo-controlled trial of oral azidothymidine (AZT) was conducted in 282 patients with AIDS or AIDS-related complex (ARC). Although significant clinical benefit was documented serious adverse reactions, particularly bone marrow suppression, were also observed. Nausea, myalgia, insomnia and more severe headaches were reported more frequently by AZT recipients. Macrocytosis developed within weeks in most subjects. Anemia, with reductions of >25% in baseline hemoglobin levels, occurred in 38% of AZT recipients and 13% of placebo recipients (p <0.05). Hemoglobin levels below 7.5 g/dl developed in 24% of AZT recipients and 4% of placebo recipients (p <.001). 21% of AZT recipients and only 4% of placebo recipients required multiple transfusions (p <.001). Neutropenia of less than 500 cells/mm^3 occurred in 16% of AZT recipients compared to 2% of placebo recipients (p <.001). Patients who entered the study with low T4 lymphocyte counts, low serum vitamin B12 levels, low hemoglobin, or low neutrophil counts were more likely to experience hematologic toxicity. Acetominophen co-administration was also associated with a higher frequency of hematologic toxicity. Although a subset of patients has tolerated AZT for an extended period with few problems, the drug should be administered with caution because of its recognized toxicities and the limited experience acquired with the drug to date.

T.8.5 Ribavirin delays progression of the lymphadenopthy syndrome (LAS) to the acquired immune deficiency syndrome (AIDS).

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Ribavirin, a synthetic guanosine nucleoside analogue has in vitro activity against the human immunodeficiency virus (HIV). Ribavirin's role in preventing progression of LAS to AIDS was evaluated in a randomized, double-blind, placebo-controlled, multicenter trial. One hundred and sixty-three homosexual men with LAS were treated with oral ribavirin or placebo for 24 weeks, followed by no treatment for four weeks. All were HIV culture positive, had lymphadenopathy for six months or more, hematocrits ≥ 35% and fewer than 500 (± S.D. of the method) T4+ cells. Those with chronic symptoms of HIV infection (diarrhea, fever, thrush, weight loss) were excluded. Fifty-two received 800 mg of ribavirin daily and none developed AIDS; 6/55 (11%) given 600 mg/day of ribavirin and 10/56 (18%) taking placebo developed AIDS (p=0.007). Difference in outcome correlated with ribavirin plasma levels. This therapeutic effect was not explained by differences in T4+ cells or hematocrit at initiation of therapy. Qualitative HIV cultures remained positive and measured immunologic function did not increase in the treated groups. Three of 107 (2.8%) receiving ribavirin discontinued treatment because of insomnia or nausea/vomiting. Ribavirin was associated with a mild compensated anemia; no one required a blood transfusion. There was one death, AIDS-related, in the placebo group. Prolonged ribavirin therapy is well tolerated and delays the progression to AIDS of immunologically compromised men with LAS. Ribavirin deserves further study as a therapeutic agent for HIV infection.

T.8.6 Serum HIV Core Antigen in Symptomatic ARC Patients Taking Oral Ribavirin or Placebo.

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We measured HIV p24 core antigen (AG) in serial sera of symptomatic ARC patients as part of a multicenter, placebo-controlled, randomized trial of oral Ribavirin. Fifty-six men with ARC were randomized to placebo or one of two oral ribavirin regimens. AG was measured by sandwich enzyme immunoassay in samples taken at weeks 0 and 12. Counts of T4 lymphocytes and culture for HIV were performed at both times. Mean AG levels (+/- S.E.) were:

Week	N	Placebo	600 mg qd	800 mg qd
0	56	275 +/- 81	325 +/- 118	174 +/-51
12	49	203 +/- 60	382 +/- 114	324 +/- 85

Our data fail to show a statistically significant difference in mean AG levels of ribavirin-treated ARC patients and placebo controls (p=0.28 by ANOVA; p=0.19 by t test comparing drug and placebo). There was no significant difference in change in mean T4 cell counts when comparing patients on drug with those on placebo (p=0.35, t test). Culture positivity was similar in drug and placebo groups at week 0 (29/37 drug; 14/19 placebo) but was different at week 12 (23/33 drug; 15/16 placebo; p=0.08 FET). Five patients developed AIDS by Week 12. Seventeen of 49 men tested on two occasions had no AG at either time. These data are qualified by small numbers and by 7 drop-outs. We will present data on 150-200 patients, measured at 5 points over 24 weeks, with quantitative aspects of culture. In sum, we found no effect of oral ribavirin on serum AG levels; our data suggest that an effect on virus culture positivity may be present.

Immunology—HIV-Specific Cytotoxicity

T.9.1 HIV env- and gag- Specific Cytotoxic T Lymphocytes (CTL's) in Seropositive Subjects

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Using recombinant vaccinia viruses to express HIV genes, we have detected circulating HIV-specific CTL's in homosexual males seropositive for the AIDS agent. EBV immortalized B cell lines established from 8 seropositive subjects and 5 seronegative controls were infected with recombinant vaccinia viruses expressing the HIV env (VAC/env) or gag (VAC/gag) gene, or a control vaccinia vector expressing the bacterial lac Z gene (VAC/lac), and used as targets in a chromium release assay. Freshly isolated autologous peripheral blood mononuclear cells were used as effector cells. HIV env- and gag- specific cytotoxic responses were detected in seropositive subjects, but not seronegative controls. At an effector: target ratio of 100:1, mean specific lysis of the different vaccinia-infected target cells in seropositive subjects was a) VAC/env 37.5 ± 6.2% ($p<.005$ vs VAC/lac) b) VAC/gag 17.2% ± 3.8% ($p<.05$ vs VAC/lac) c) VAC/lac 11.2 ± 3.3%. For seronegative subjects, these values were a) VAC/env 8.6 ± 1.2% b) VAC/gag 7.8 ± 1.1% c) VAC/lac 7.7 ± 1.1%. The env - specific cytotoxic response was inhibited by 67-100% by addition of a CD3-specific monoclonal antibody, indicating that the effector cells are T lymphocytes. This demonstration of HIV-specific cytotoxicity in seropositive individuals should prove useful in further investigating the immunopathogenesis of AIDS and in evaluating vaccine strategies.

T.9.2 Detection of HLA Restricted Human Immunodeficiency Virus (HIV) Envelope Antigen-Specific Cytotoxic Lymphocytes (CTL).

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Because cell-associated virus may be important in transmission and pathogenesis of HIV infection, vaccine-induced protective immunity may require induction of CTL killing of infected cells. To measure HIV envelope-specific CTL, peripheral blood mononuclear cells from asymptomatic HIV seropositive individuals were stimulated in vitro for 5 days with autologous, irradiated, HIV infected T-lymphoblasts. Human skin fibroblast target cells matched to the donor at one or more HLA-A or B loci, or mismatched, were infected with recombinant vaccinia containing the whole envelope gene of the HTLV-III_B strain of HIV. The same target cells infected with recombinant vaccinia lacking this insert served as controls. Targets were labelled with ^{51}Cr and at 19 hours after infection were incubated with effector cells at an effector:target ratio of 25-30:1 for 4 hrs. ^{51}Cr release was then measured and the percent lysis calculated. HIV envelope-specific lysis was determined by subtracting the results with the control from those with the envelope recombinant. Six of 8 donors tested showed significant ($p<0.05$) HIV envelope-specific lysis (mean % lysis 9.4 +/- 2.2). Cells from HIV seronegative donors did not show significant lysis. Among donors showing positive responses, 8 of 12 matched but only 2 of 9 mismatched targets were lysed ($p=0.05$). Memory cells capable of developing HLA-restricted, HIV envelope-specific cytotoxic activity are present in the peripheral blood of some asymptomatic, HIV infected individuals. HIV envelope antigens can serve as targets for these responses and measurement of CTL may be an important part of evaluation of the immunogenicity of candidate vaccines.

T.9.3 Cytotoxic T Cells Directed Against Target Cells Expressing HIV-1 Proteins

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We previously detected HIV-specific cytotoxic T cells (CTL) in peripheral blood mononuclear cells (PBMC) of healthy HIV seropositive individuals as well as 2 AIDS patients who had received bone marrow (BM) transplants from their HIV seronegative identical twins. HIV-specific CTL activity was not found in PBMC of HIV seronegative individuals or in non-transplanted AIDS patients (2nd Intl Conf AIDS). In order to determine which viral proteins are important in the detection of HIV-specific CTL responses, recombinant vaccinia viruses expressing different products of the HIV genome were utilized. PHA-stimulated PBMC or EBV-transformed B cells were infected with recombinant vaccinia viruses expressing either gp120 and 41 (env), gp120 alone (env), or gp55 (gag) and used as targets in a 4 hour ^{51}Cr-release cytotoxicity assay. Cells infected with a vaccinia vector that contained a bacterial lac gene were used as a control. PBMC obtained from healthy HIV seropositive individuals or a cohort of 12 AIDS patients participating in a study of AZT used in combination with BM transplantation, served as effector cells. Most CTL activity was detected against the env region (15-48% specific lysis at an effector:target ratio of 100:1) although lysis of target cells expressing gp55 was also seen. HIV was sporadically isolated from PBMC of most of the individuals with CTL activity. Given the fact that in vitro priming was unnecessary to elicit CTL responses, these data suggest that HIV specific CTL are stimulated in vivo and may be effective in suppressing viral replication. These studies have potentially important implications in the delineation of the nature of a protective immune response in HIV infection and in devising strategies for vaccine development.

T.9.4 Gp120-Specific Cell-Mediated Cytotoxicity in Patients Exposed to HIV

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As part of an ongoing investigation of cellular anti-HIV reactivities, we examined the ability of peripheral blood mononuclear cells (PBMC) obtained from patients at various stages of disease to directly lyse cells bearing only gp120 determinants. Autologous CD4 cells were coated with purified HTLV-III_B gp120 and used as targets in 4-hour ^{51}Cr release assays for cell-mediated cytotoxicity (CMC). Gp120-specific CMC was apparent in HIV seropositive individuals at all stages of disease. Levels of CMC were highest in asymptomatic patients while ARC and AIDS patients exhibited only sporadic and low CMC. The activity was not MHC-restricted and was mediated by a $CD3^-$, $CD4^-$, $CD8^-$, $CD16^+$ population of effector cells. Although not strictly Interleukin 2 (IL-2)-dependent, CMC was greatly augmented by exogenous IL-2. Cold target competition studies revealed that anti-gp120 effector cells also recognized K562 targets. Taken together, these results suggest that a sub-population of 'NK-like' effector cells, not present in seronegative individuals, mediates the destruction of gp120 coated targets. The antigen receptor on these cells recognizes 'group' determinants, since CD4 targets coated with purified gp120 from the widely divergent HTLV-III_{RF} isolate were lysed to the same degree as cells coated with HTLV-III_B gp120.

These results not only document the presence of virus-specific cellular cytolytic elements present in HIV seropositive individuals but also highlight gp120 as a target antigen for immune cytolysis. Additionally, the ability of gp120 adsorbed CD4 cells to serve as targets for CMC suggests a possible mechanism of immunopathogenesis in which lympholysis might occur in the absence of infectious virus spread.

T.9.5 Cytotoxic T Cells, that Recognize Human Immunodeficiency Virus (HIV) Envelope Glycoproteins, Isolated from Chimpanzees Immunized with a Recombinant Vaccinia Virus Expressing HIV Glycoproteins

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Little is known concerning T cell mediated immunity to HIV. However, we previously reported that a recombinant vaccinia virus, v-env5, expressing HIV envelope (env) glycoproteins gP41 and gp110 induces T helper cells in macaques, that recognize HIV by proliferating and by producing interleukin-2. It was not determined, however, whether immunization with such a recombinant virus can also prime HIV specific cytotoxic T cells (CTL). In this study, immunization of chimpanzees, the closest relative of man, with v-env5 (but not with a recombinant vaccinia virus that expresses a herpes simplex virus glycoprotein) resulted in the generation of T helper cells that proliferate following stimulation with HIV or with purified env glycoproteins. In addition, cytotoxic T cell clones were also isolated from v-env5 immunized chimpanzees following stimulation of lymphocytes with env glycoproteins. These CTL clones lyse autologous target cells infected with v-env5 but not with parental vaccinia virus. Our results thus indicate that immunization of chimpanzees with a recombinant vaccinia virus expressing HIV envelope glycoproteins results in the generation of HIV specific T helper cells and CTL and also that HIV envelope glycoproteins serve as target antigens for cytotoxic T cells of primates. HIV specific T helper cells and CTL, such as those we have demonstrated, may play a role in limiting dissemination of HIV or preventing the development of AIDS.

T.9.6 HIV Antibodies in Human Sera Induce Cell-mediated Lysis of HIV-Infected Cells.

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The capacity of human immunodeficiency virus (HIV) antibody-positive sera to recruit non-immune lymphocytes to lyse HIV-infected T cell lines was investigated. Sera from twenty-seven asymptomatic homosexual men with normal CD4/CD8 cell ratios were shown by ELISA to have antibodies to the whole HIV. At dilutions between 10^{-2} and 10^{-5}, twenty-two of these sera caused lysis of HIV-infected target cells (MOLT-4f and CEM-CCRF) above the level of spontaneous lysis caused by either peripheral blood lymphocytes (PBL) alone, or lysis of HIV-antibody-coated uninfected target cells in the presence of added PBL. HIV-antibody negative sera did not cause lysis. Fractionation of the HIV-antibody positive sera on protein-A affinity columns showed that the ADCC-inducing molecule resided in the Ig-fraction. Thus, identification of the extra cytotoxic activity in the IgG fraction is indicative of antibody-dependent cellular cytotoxicity (ADCC). Varying capacity to cause ADCC was observed among the different HIV-antibody positive sera. Using radioimmunoprecipitation-SDS-PAGE analysis with [^{35}S]-methionine-labeled HIV-infected cells, it was shown that antibody to the HIV envelope protein, gp^{120} was present in reactive, but not in ADCC inactive, sera. There was no correlation, however, with presence or absence of antibodies to p24, p55 or gp41 antigens.

These results suggest that HIV envelope proteins play an important role in HIV-specific responses.

TUESDAY, JUNE 2

Psychosocial—Psychosocial Research: At Risk Populations

T.10.1 The primary prevention of AIDS: An urgent research agenda.
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AIDS is a fatal and incurable disease that has already had an unprecedented impact on the health and social structure of our society, and the adverse effects of the epidemic will intensify as those who are already infected develop clinical disease. These facts lend urgency to the need to develop more effective approaches to preventing the further spread of infection.

AIDS is a behaviorally transmitted disease, and culture-specific behavioral interventions are the only known approach to primary prevention. In order to develop a more effective public health response there is a need to greatly enhance our pursuit of the following research agenda:

1. Population based epidemiologic studies to inform us on the distributions of HIV infection, and on the distributions of high risk behaviors and their antecedents, in various segments of the population, and,

2. Health education intervention studies to reveal the most cost-effective approaches to reducing high risk behaviors, and to tailoring preventive strategies to those segments of the population (such as the black and hispanic minorities) that are at disproportionely high risk.

This research agenda is staggering in size, since these issues should be addressed in many cultural and language settings throughout the world, not just in the United States. There is a need for more fiscal resources to support these efforts, and for more health scientists to become involved in their pursuit.

T.10.2 Persistence and Change in Sexual Behavior and Perceptions of Risk for AIDS among Homosexual Men.
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A longitudinal study of modifications in sexual behavior among asymptomatic homosexual men (n=161) in New York City was conducted. Participants were interviewed at two time points (T1 and T2) six months apart. Based on respondents' reports of their behavior during a recent "typical" month, the riskiness of their sexual behavior was scored from 0 to 4. Scores were based on available epidemiological evidence concerning sexual behaviors associated with HIV associated conditions. Respondents were also asked to rate their own behavior on a scale from 1 to 10 based on how risky they thought their current practices were in terms of contributing to their chances of getting AIDS.

When change between T1 and T2 was examined, a number of patterns emerged. For almost half (47%) of the respondents there was no change in their risk rating. About one-third (36%) received a lower risk rating at T2, and the remaining men (17%) received a high risk rating. A full 41% of the men studied were practicing risky sex at both assessment points, while only 29% were engaging only in safe sex at the two time points. The remaining 30% had shifted categories (20% risky at T1, safe at T2; 10% safe at T1, risky at T2).

When respondents' subjective ratings of the riskiness of their behavior were compared with the objective scores, it was determined that as many as four out of every five men engaging in risky sexual behavior may be underestimating the danger inherent in their behavior.

The implications of these findings for future public health efforts will be discussed.

T.10.3 KNOWLEDGE OF H.I.V. CONTAMINATION MODALITIES AND ITS CONSEQUENSE ON SEROPOSITIVE PATIENTS BEHAVIOUR.
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We made investigation on behaviour of 150 patients informed of their H.I.V. seropositivity, Living on French Riviera, which is the second French place for A.I.D.S. rate. Characteristics of this population are the following : drug addicts : 100 (67 %), homo and bisexuals : 32 (21%) exclusive heterosexuals : 10 (6,5 %), transfused : 8 (5,5 %) ; median age (17-79) : addicts : 25, homo and bisexuals : 29, transfused : 41. For each group specific contamination risk was known on an average of 16 months for addicts, 35 months for transfused patients. Drug addicts stopped syringe exchange in 51 % of cases, drug (héroïn) in 36 % and use condoms : 33 %. Among 73 % of homosexuals who carry on sexual practices, 37 % use condoms. almost of heterosexuals who carry on sexual activity use protective mean (4/5). In this study, transfused population is not significant because of lack of seropositivity knowledge and lack of sexual activity in all patients related to severity of initial disease.

Although these results appear disappointing, they do signify a real change in practice of risk patients, which justify repetitive and specific public information conciousness being heterogenous according to the groups.

T.10.4 Preventing Human Immunodeficiency Virus Contagion Among Intravenous Drug Users: The Impact of Street-Based Education on Risk-Behavior

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An evaluation of a street-based, AIDS prevention and health education project directed at out-of-treatment intravenous drug users (IVDUs) was conducted in San Francisco. Two waves of IVDUs were interviewed and data obtained on drug use and medical history, sexual practices, needle-hygiene, beliefs and knowledge about AIDS transmission, and HIV serology performed. Each wave contained respondents who were sampled from non-clinical populations of IVDUs not connected with treatment programs and clinical populations of IVDUs enrolled in 21-day drug-detoxification programs. The first wave (n=438) was conducted during Winter/Spring, 1986 and the second wave (n=500) was conducted during Winter/Spring 1987. The intervention--which placed "community health outreach workers" in San Francisco neighborhoods with large numbers of IVDUs--was implemented at the approximate mid-point between observations.

Preliminary findings suggest significant change between waves in adoption of the recommended needle-hygiene procedures. Additional findings include reported reductions in needle-sharing, increased use of condoms, and increased AIDS knowledge. HIV infectivity was significantly higher among the non-clinical group (16%) than the clinical group (7%) in the 1986 wave. Preliminary results suggest an approximate doubling of HIV infectivity between the 1986 and 1987 waves.

T.10.5 Determinants of Current Psychiatric Disorder in AIDS Spectrum Patients.
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Current psychiatric status was examined at diagnosis in gay men with AIDS (A=90) and ARC (ARC=40), and compared with that of healthy gay men (H=149) in New York City. Standard psychiatric interviews, using structured interview schedules, were conducted to obtain D.S.M.-III diagnoses by reliable interviewers (Kappa = ~.70). 42% of the entire sample had any current disorder--chiefly adjustment disorder (81% of disorders). Rates were higher for the A (52%) and ARC (63%) groups than for the H group (31%). The A, and especially, ARC groups also exceeded the H group on self-reported psychological distress on the Brief Symptom Inventory ($p=.001$). Hierarchical multiple regression analysis was performed to identify the determinants of psychiatric disorder. The resulting equation accounted for 20% of the variance. A series of significant predictors ($p<.01$) were associated with the following increments in explained variance: history of past major affective or anxiety disorder (3%); diagnosis of AIDS or ARC (5%); number of AIDS spectrum physical symptoms (4%); and extent of self-reported psychological distress (9%). Reactive psychiatric disorders are a common and highly treatable complication of AIDS and ARC-- which may be readily detectable from the patient's own report.

T.10.6 Two-Year Longitudinal Study of Behavioral Risk Reduction in a Cohort of Homosexual Men
JILL G. JOSEPH*, S. Montgomery*, R.C. Kessler*, D.G. Ostrow*, C.A. Emmons*, J.P. Phair**, *University of Michigan, Ann Arbor, MI, USA, **Northwestern University, Chicago, IL, USA

A cohort of approximately 650 homosexual Chicago men provided behavioral and psychosocial data from mid-1984 to mid-1986. A four level objective risk index was constructed and validated using HIV serological data. This index summarizes number and type (e.g. monogomous; anonymous) of sexual partners, frequency of receptive anal intercourse, and use of condoms. Although 35% of the cohort was categorized as at high risk originally, by Wave 4 this was true of only 6.0%. Similarly, while 6.1% were originally completely avoiding risk behaviors, two years later 13.4% were doing so. Components of the health belief model at Wave 1 were used as predictors in a series of multiple logistic regressions which examined subsequent risk reduction. Indices were constructed to quantify knowledge of AIDS, perceived risk, perceived efficacy of behavioral change, social network characteristics, peer norms, difficulties with sexual impulse control, and beliefs in technological solutions to the AIDS crisis. Of these, knowledge ($p<.01$-$.05$), peer norms ($p<.01$-$.02$), and difficulties with sexual impulse control ($p<.01$-$.02$) were consistently predictive of behavioral risk reduction. This provides evidence for the role of cognitive, social and psychological factors in behavioral risk reduction.

Roundtable Discussions

T.11

Access Issues Associated with AIDS:
Discrimination, Services, Care

Panel Moderator: Jeffrey Levi
National Gay and Lesbian Task Force
Washington, D.C.

Tom Stoddard, Lambda Legal Defense and Education Fund, New York, New York

Ben Schatz, National Gay Rights Advocates, San Francisco, California

Tim Westmoreland, Council House Subcommittee on Health and the Environment, Washington, D.C.

Adam Carr, Victorian AIDS Council, Richmond, Australia

Katy Taylor, New York City Human Rights Commission, New York, New York

T.12

Use of AZT in HIV Infections

Panel Organized By: John La Montagna
National Institute of Allergy and Infectious Diseases
Bethesda, Maryland

Douglas Richman, Veterans Administration Medical Center, San Diego, California

Paul Volberding, University of California, San Francisco, San Francisco, California

Margaret Fischl, University of Miami, Miami, Florida

Sandra Lehrman, Burroughs Wellcome Company, Research Triangle Park, North Carolina

T.13

Encouraging Physician Counseling for AIDS Prevention

Panel Organized By: Neil R. Schram
LA City/County AIDS Task Force
Los Angeles, California

David McEwan, Honolulu Medical Group, Honolulu, Hawaii

Brian Willoughby, Vancouver, Canada

Mark Behar, Milwaukee, Wisconsin

Alan Novick, Yale University, New Haven, Connecticut

T.14

Legal, Ethical and Public Policy Issues:
International Perspective

Panel Moderator: Richard Riseberg
Public Health Service, HHS
Washington, D.C.

Ronald Robertson, Department of Health and Human Services, Washington, D.C.

LeRoy Walters, Joseph and Rose Kennedy Institute of Ethics, Washington, D.C.

Bernard Dickens, University of Toronto, Toronto, Canada

Harvey V. Fineberg, Harvard University, Boston, Massachusetts

Sev Fluss, World Health Organization, Geneva, Switzerland

Michael D. Kirby, Court of Appeals, New South Wales, Australia

Eric Matthews, University of Aberdeen Kings College, Aberdeen, Scotland

Helen Roscam-Abbing, University of Limberg, Maastricht, The Netherlands

Brenda Almond, The University of Hull, Hull, England

T.15

Psychological Distress and Maintenance of
Behavior Change in HIV Illness

Panel Organized By: Peter Bridge
ADAMHA
Bethesda, Maryland

Panel Moderator: Ellen Stover
National Institute of Mental Health
Rockville, Maryland

John Newmeyer, CEO Youth Projects, Inc., San Francisco, California

Peter M. Davies, South Bank Polytechnic, London, England

Jeff Moulton, Langley Port Psychiatric Institute, San Francisco, California

David Ostrow, University of Michigan, Ann Arbor, Michigan

Thomas Coates, University of California - San Francisco, San Francisco, California

Biology of HIV

T.16.1 The AIDS Virus Genomes: Structure and Function.

Flossie Wong-Staal, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

T.16.2 Molecular Basis for Approaches for Diagnostic, Therapeutic, and Prophylactic Measures for Control of AIDS.

WILLIAM A. HASELTINE**, JOSEPH SODROSKI*, CRAIG ROSEN*, ERNEST TERWILLIGER*, ANDREW DAYTON*, ROBERTO PATARCA*. *Dana-Farber Cancer Institute, Dept. of Biochemical Pharmacology, Harvard Medical School, and **Harvard School of Public Health, Dept. of Cancer Biology, Boston, MA.

The studies of the replication cycle, genetic regulatory pathways and mechanisms of cellular cytopathicity of the AIDS virus will be presented in the context of their potential for the development of improved techniques for the control of the disease.

Specifically, studies of the cis and trans elements of the viral genome will be presented. In this study, the structure/function of envelope glycoprotein will also be discussed as it pertains to early steps of infection, cytopathic effect and immunoprophylactics. The potential for other viral genes as targets for anti-viral drugs, including the protease reverse transcripatase and endonuclease integrace genes will also be discussed.

T.16.3 Genetic Variability of the AIDS Viruses.

Simon Wain-Hobson, Institut Pasteur, Paris, France.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

T.16.4 The Immunobiology of the External Envelope Viral Glycoprotein

THOMAS J. MATTHEWS*, SCOTT D. PUTNEY**, JAMES R. RUSCHE**, ROBERT C. GALLO***, DANI P. BOLOGNESI*, *Duke University Medical Center, Durham, NC, **Repligen Corporation, Boston, MA, ***National Institutes of Health, Bethesda, MD

The interaction of gp120 with the CD4 surface lymphocyte marker is critical for the processes of virus infection and virus mediated cell/cell fusion. We have examined the relationship between the segments of gp120 responsible for each of these activities as well as those serving as target epitopes for virus neutralization. These results will be discussed in terms of vaccine and interventive strategies for the disease.

T.16.5 EXPERIMENTAL IMMUNE ACTIVATION AGAINST AIDS VIRUS IN HUMANS

D. Zagury, Z. Lurhuma, K. Mbayo, J.J. Saisun, R. Leonard, J. Bernard, M. Fouchard, B. Revail, B. Goussard, J. Wane.
Universite Pierre & Marie Curie (Paris) - Institut J. Godinot (Reims) - Faculte de Medecine de Kinshasa et INRB (Kinshasa).

The diversity of subtypes of human immunodeficiency virus (HIV) represents a major difficulty in the immune defense mechanisms against AIDS because a humoral response induced by one HIV strain may generate neutralizing Abs only against that strain and not against other HIV strains. That prompted us to investigate whether a cell mediated immune response (CMI) would overcome the subtype diversity limitations. Previous studies showed that infected T cells procead, before release of virions, through an immunogenic stage, where the cell may a) trigger a CMI and b) represent a target for a specific cytotoxic T Cell (CTL). These data rationalize our operative strategy, to trigger a CMI against HIV infection by either non infectious fixed antologous cells expressing HIV antigens at the cell surface (for seropositive immune deficient organisms) or a vaccinia recombinant (Vr) expressing Gp.160 env protein from HTLV.III-B (for seronegative organisms). After preliminary experiments on monkeys showed the innocuity of both treatments, we treated by their fixed cells infected in vitro, 2 volunteers ARC patients, followed 3 months after, by 8 others. No clinical complication whatsoever occurred up to now and immunological parameters improved significantly. We also immunized with Vr a seronegative individual (D.Z., one of us) no clinical manifestation nor immunological defect occurred during the immunization. We then immunized 10 individuals high risk seronegative immunologically normal individuals, all voluntaers. D.Z. and these individuals presented a normal vaccine course without any complication. In our presentation we will report the results of clinical and biological follow up and the degree of the immune response against different strains of HTLV.III. Finally we will discuss the scientific, ethical and economic conditions required for clinical trials of vaccines against HIV. All these researches have the full support of the Zairian Executive Council and its Ethics Committee.

Poster Session

TP.1 Correlation between Metabolism and Antiretroviral Effect of AzddThd (AZT) and ddCyd in Murine and Human Cell Systems in vitro and in vivo.

JAN BALZARINI*, R. PAUWELS*, M. BABA*, E. DE CLERCQ*, S. BRODER** and D.G. JOHNS***. *Rega Institute for Medical Research, University of Leuven, B-3000 Leuven, Belgium; **Clinical Oncology Program and ***Developmental Therapeutics Program, National Cancer Institute, NIH, Bethesda, MD 20892, U.S.A.

2',3'-Dideoxycytidine (ddCyd) is superior to 3'-azido-2',3'-dideoxythymidine (AzddThd) in suppressing the in vitro infectivity of human immunodeficiency virus (HIV) in human ATH8 cells. In contrast, AzddThd inhibits the in vitro transformation of C3H mouse (MO) cells by Moloney murine sarcoma virus (Mo-MSV) at an inhibitory dose (ID_{50}) of 0.06 μM, that is at a concentration at least 400-fold lower than the ID_{50} of ddCyd. Daily AzddThd treatment (125 mg/kg/day) of NMRI mice infected at 3 days after birth with Mo-MSV almost completely prevented MSV-induced tumor formation and resulted in a complete survival of the mice. At 25 mg/kg/day, significant delay in tumor formation and considerable prolongation of the life span of the mice was observed. In contrast, ddCyd treatment at 125 or 25 mg/kg/day only resulted in a slight delay of tumor formation, without any effect on the survival rate of the mice. Since AzddThd-5'-triphosphate (AzddTTP) and ddCyd-5'-triphosphate (ddCTP) are assumed to be the active antiretroviral metabolites in the cell, we compared the levels of these metabolites in human and murine cells. Under similar experimental conditions, lower ddCTP but higher AzddTTP levels were observed in murine L1210 cells than human ATH8 cells. Thus, the antiretroviral effect of AzddThd and ddCyd correlated well with their corresponding intracellular 5'-triphosphate levels. These findings strongly suggest that the intracellular levels of the 5'-triphosphate metabolites of 2',3'-dideoxynucleosides determine their efficacy for inhibition of retroviral infections and that the potency of these agents are greatly influenced by cell type dependent metabolism.

TP.2 A Model of Human Immunodeficiency Virus (HIV-1)

ALBERT F.BYKOVSKY, Institute of Epidemiology and Microbiology, Moscow, U.S.S.R.

We have carried out a comparative study of various strains of HIV-1, such as: LAV (obtained from Prof.L.Montagnier, Institut Pasteur, Paris, France), HTLV-III (from Dr.R.Gallo, Bethesda, USA), ARV (from Dr.J.Levy, San-Francisco, USA), the latter two were received from Prof.V.M.Zhdanov. The molecular organization of subvirion components of HIV-1 was examined using the high-resolution electron microscope. We studied as components as the core, ribonucleoprotein, the reverse transcriptase, gp 120, gp 41, p 24, p 18 and p 13. The diameters of the virions with single core were about 140-160 nm, but the diameters of the virions with two cores were about 200-250 nm.

The cores were rod- or conic-shaped and usually were located excentrically. Rod-shaped cores had the size of 130-150x40-50 nm, conic cores had the height of 100-130 nm and the diameters of 60-70 nm in the upper part and 10-15 nm in the base one. The core shell contained spherical structures with the size of 6-7 nm x 3-4 nm. The nucleoids, consisting from ribonucleoprotein threeds (2 nm in diameter), were packaged in special way into loops (diameter of 5-6 nm).

The intermediate layer of virions contained globular structures (2-3 nm). Spherical structures on the surface of virions (10-11 nm) contained central channel (2 nm).

"Minimal forms" of HIV-1 (diameter 50-70 nm) were also found. The visualization of components of HIV-1 let us construct a stereo model of the virus.

TP.3 Monoclonal Antibodies to Peptides of the gp41 Molecule Neutralise Variant Isolates of HIV

A.G. DALGLEISH, R.C. KENNEDY*, P.C. CLAPHAM**, T.C. CHANH*, G.R. DREESMAN* and M. MALKOVSKÝ, Retrovirus Research Group, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England; *Department of Virology and Immunology, Southwest Foundation for Biomedical Research, San Antonio, TX 78284, USA; **Chester Beatty Laboratories, Institute of Cancer Research, Fulham Road, London SW3 6JB, England.

We have previously shown that rabbit antibodies raised against HIV envelope peptides neutralise virus infectivity in vitro (Chanh et al., EMBO J. 5, 3065-3071, 1986; Kennedy et al., Science 231, 1556-1559, 1986). We now show that monoclonal antibodies against 3 different gp41 peptides all neutralise different isolates of HIV as determined by syncytia, pseudotype, reverse transcriptase and long term infectivity assays. This data has important implications for the development of anti-HIV vaccine.

TP.4 In Vitro Infection of Primate Lymphocytes by HIV-1 and Expression of CD4 Epitopes

MYRA O. McCLURE*, Q. SATTENTAU**, P. BEVERLEY**, J. HEARN***, A.J. ZUCKERMAN****, R.A. WEISS, *Chester Beatty Laboratories, **Department of Human Tumour Immunology, University College London, ***Institute of Zoology, ****Department of Medical Microbiology, London School of Hygiene and Tropical Medicine, London.

Peripheral blood monoclonuclear cells (PMB) from a number of primate species were infected in vitro with HIV-1.

PBM were phenotyped for expression of epitopes of the CD4 antigen with a panel of CO4 monoclonal antibodies (Mabs) by indirect immunofluorescent staining and FACS analysis. The greater the divergence of the primate species from man, the fewer epitopes were conserved, and only one epitope was consistently represented in all species tested. This could be detected by the CD4 Mabs leu 3a, MT310, F101-65 and 94b1, all of which strongly inhibit the virus CD4 interaction in human cell lines. Infection of the primate PBM with supernatants of HIV-1 was tested after stimulation with PHA and IL-2. Samples of infected PBM or supernatants from these cultures induced a cytopathic effect in the C8166 $CD4^+$ indicator human cell line. Preliminary data also show induction of RT activity in infected PBM and the presence of p18 by immunofluorescence. These data may indicate primate species which could be susceptible to infection. In vivo tests are in progress. They may also indicate which part of CD4 is essential for virus binding.

TP.5 Characterization of a Monoclonal Antibody Specific for the HIV-I Precursor Glycoprotein.

B. KRUST[1], A. G. LAURENT[1], A. LE GUERN[2], O. JEANNEQUIN[2], L. MONTAGNIER[1] and A. G. HOVANESSIAN[1]. [1]Unité d'Oncologie Virale, [2]Hybridolab, Institut Pasteur, 25, rue du Dr. Roux, 75724 Paris Cédex 15, France.

HIV-1 infected MOLT4-T4 cells provide an efficient system for the production of cellular precursor gp160 of HIV envelope glycoproteins, gp120 and gp41.

The precursor gp160 was purified on an immuno-affinity column containing antibodies from sera of HIV-1-seropositive patients. The precursor gp160 was then isolated by preparative polyacrylamide gel electrophoresis. Two out of 4 BALB/C mice immunized with these purified preparations of gp160, developed specific circulating antibodies after 5 injections at 2 weeks interval. A hybridoma cell line was subsequently isolated producing monoclonal antibody (IgG1, κ) specific for gp160. This monoclonal antibody can immunoprecipitate specifically gp160 present in HIV-1-infected cells. In an immuno-blotting assay, it identifies mainly gp160 and manifests a slight affinity for the mature glycoprotein, gp120. The monoclonal antibody is probably directed against an epitope in the polypeptide residue of gp160 since it can recognize a 90,000 Mr deglycosylated polypeptide, product of gp160 digestion by Endo H. It does not cross-react with any protein of HIV-2 by immunoblot or immunoprecipitation assays. By virtue of its specificity, the monoclonal antibody might provide a powerful probe to detect gp160 in cells and tissues which might express partially the HIV-1 genes.

TP.6 Evidence for lentiviral etiology in an epizootic of lymphoma and immunodeficiency in stump-tailed macaques (Macaca arctoides)

LINDA J. LOWENSTINE*, N.W. LERCHE*, M. JENNINGS**, J. YEE**, A. UYEDA**, M. GARDNER**, et al., *California Primate Research Center, **Schools of Veterinary Medicine and Medicine, University of California, Davis, CA, USA.

Infections of nonhuman primates with simian T-lymphotropic lentiviruses (STLV-IIIs) serologically related to HIV and HIV-2 provide important models for human AIDS. Reports in the literature suggest that these viruses are endemic in some populations of African monkeys, e.g. African green monkeys (Cercopithecus aethiops) and sooty mangabeys (Cercocebus atys), but do not cause disease. Natural infections in captive macaques are rare but inoculation of macaques with isolates from macaques or African monkeys causes an AIDS-like disease. Retrospective studies of a naturally occurring epizootic of immunosuppression and lymphoma in stump-tailed macaques (StM) that occurred between 1976 and 1978 at the California Primate Research Center have revealed that sera from many StM reacted strongly with HTLV-III (HIV); LAV-2 (HIV-2); STLV-III (macaque and sooty mangabey). None of the sera reacted with the simian immunosuppressive type-D retroviruses which are the common cause of epizootic simian AIDS (SAIDS) in macaques in the U.S. Inoculation of a juvenile rhesus (M. mulatta) with a lymph node homogenate from a StM that died in 1977 of lymphoma produced lymphadenopathy and decreased T4/T8 ratio. The animal developed antibodies cross reactive with human and simian lymphotropic lentiviruses. Virus recovered from this rhesus had Mg++ dependent reverse transcriptase and the ultrastructure of a lentivirus. This documents the first naturally occurring propagating epizootic of lentivirus associated SAIDS in captive macaques and provides an additional isolate for comparison with known human and simian lentiviruses.

TP.7 Absence of HTLV-IV in Central Africa

PHYLLIS KANKI*, J. ALLAN*, F. BARIN**, M. ESSEX*, *Harvard School of Public Health, Boston, MA, **University of Tours, Tours, FRANCE.

HTLV-IV was first described in Senegal and has been shown to be prevalent in most countries of West Africa where reports of AIDS cases are still infrequent. In contrast, AIDS and HTLV-III/HIV are observed at high and increasing rates in discrete regions of Central Africa. This study was conducted to assess the prevalence of HTLV-IV in 7 countries of Central Africa and to determine any association with AIDS or a related disorder. Serum samples from healthy controls, tumor patients, ARC, tuberculosis, STD patients, and AIDS were kindly provided to us as a collaborative study with T. Quinn, N. Clumeck, F. Mawovondi, I. Lausen, D. Zagury, L. Thiry, J. Craighead, C. Saxinger, and L. Falk; Zaire, Cameroon, Zambia, Kenya, Tanzania, Burundi, and Uganda were represented in the sample population.

All 1,430 serum samples were analyzed by radioimmunoprecipitation and SDS/PAGE and immunoblot for antibodies to HTLV-IV. The cross-reactivity between HTLV-IV and HTLV-III/HIV antigens has been well documented and appears to be the strongest in gag and pol encoded antigens. Therefore, a positive HTLV-IV response was distinguished by a specific response to the env antigens of HTLV-IV, the gp160/120 and gp32 (transmembrane). NONE of the 1,430 samples analyzed demonstrated antibodies to the env-related antigens of HTLV-IV; in HTLV-III/HIV antibody positive samples, cross-reaction to the gag and pol antigens of HTLV-IV was frequently observed.

HTLV-IV was not detected in 7 Central African countries surveyed, whereas HTLV-III/HIV in association with AIDS and related disorders was quite common. Further study on these two viruses of apparently differing pathogenicity will be important to our general understanding of various members of the HTLV family and how they have evolved.

TP.8 HIV Infection of B Lymphoblastoid Cell Lines

JAMES E. MONROE*, G. LENOIR**, C. MULDER*, *UMMS, Worcester, MA, USA, **International Agency for Research on Cancer, Lyon, FRANCE

We examined the susceptibility of B Lymphoblastoid cell lines to HIV infection. A series of EBV genome-negative and EBV-converted Burkitt Lymphoma cell lines, and other EBV-infected cell lines, exhibiting both permissive and non-permissive EBV infection, were studied. Initial studies showed that only 1 of 4 EBV-negative Burkitt Lymphoma cell lines and 10 of 20 EBV-positive cell lines could be infected with HIV-IIIB. HIV infection was monitored using reverse transcriptase and cytoplasmic RNA dot-blot assays.

Further studies using two different strains of HIV (IIIB, RF) and a LAV 2 strain (NºI-532) followed. The C-8166 syncytia assay was also used to monitor infection. Twenty-two of 24 cell lines could be infected with at least one of the three virus strains. In certain cell lines, virus production was very low and detectable only by the syncytia assay. Each cell line which could be infected with HIV was found to express T_4 surface antigens.

It is clear from this study that prior EBV infection has no major effect on HIV susceptibility. Southern blot analysis of DNA extracted from long-term, HIV-nonproducing cell lines detected integrated HIV genomes. This study indicates that T_4-positive B lymphoblastoid cells may serve as a reservoir for latent HIV infection, even in the absence of EBV infection.

TP.9 Detection of HIV-Specific Sequences Using in Vitro Nucleic Acid Amplification and Oligonucleotide-Based Affinity Chromatography

THOMAS R. GINGERAS*, D.D. RICHMAN**, G.R. DAVIS*, AND D.Y. KWOH*, *The Salk Institute Biotechnology/Industrial Associates, Inc., La Jolla, CA, USA, **University of California, San Diego School of Medicine, La Jolla, CA, USA.

The polymerase chain reaction (PCR) protocol, first described by Siaki et al. [Science (1985) 230:1350-1354], permits a 10^6-fold increase in the copy number of a 350 bp region from the env gene of the HIV RNA genome. The products of this in vitro amplification can be labeled by incorporation of ^{32}P-dCTP during the last cycle of amplification. Although the labeled nucleotides can be incorporated into both HIV-specific and human-host cell-specific sequences, the labeled HIV-specific fragment can be detected by a rapid and simple hybridization procedure using support-bound, HIV-specific oligonucleotides. This protocol has been applied to the detection of HIV present in cultured cell lines (CEM) and in clinical samples derived from a longitudinal study of a cohort of 240 homosexual men at various degrees of risk for AIDS. Results from the application of this detection protocol to these samples will be discussed.

TP.10 Immunoaffinity Purification of the Major Envelope Glycoprotein from HTLV-III-Infected H9 Cell Culture Media.

STEPHEN W. PYLE*, W.G. ROBEY**, J.W. BESS, JR.*, P.J. FISCHINGER**, R.V. GILDEN*, L.O. ARTHUR*, *Program Resources, Inc., NCI-Frederick Cancer Research Facility (FCRF), Frederick, MD 21701, **Office of the Director, Virus Control Unit, NCI-FCRF, Frederick, MD 21701, USA.

Purified external envelope glycoprotein, gp120, of the human immunodeficiency virus (HIV), the name proposed for the retrovirus causually associated with acquired immune deficiency syndrome (AIDS), has been shown to induce the formation of neutralizing antibodies when inoculated into laboratory animals and is, therefore, being evaluated as a prototype vaccine. The gp120 is not tightly associated with the virus and is shed into the culture fluids used to propagate HTLV-IIIb-infected H9 cells. We have utilized an immunoaffinity resin, prepared by coupling IgG from AIDS patient sera to Sepharose 4B, to purify gp120 from this culture fluid. In a typical run, virus is removed from the culture fluid by continuous-flow ultra-centrifugation, and 144 liters of the fluid is chromatographed over the immunoaffinity resin. After washing, bound HTLV-IIIb envelope glycoprotein was eluted with low pH buffer. Following extensive dialysis against distilled water, the gp120 was further purified by polyacrylamide gel electrophoresis, HPLC or differential precipitation. This purified gp120 induced both precipitating and neutralizing antibodies in laboratory animals and will provide a valuable reagent in AIDS vaccine research and HIV envelope studies.

Research sponsored, at least in part, by the National Cancer Institute, DHHS, under Contract Number NO1-CO-23910 with Program Resources, Inc.

TP.11 Expression in E. coli of open reading frame gene segments of Human B-lymphotropic virus (HBLV)

MING-CHIU FUNG*, S.C. FUNG*, S.F. JOSEPHS**, M.L. BERMAN***, F. WONG-STAAL**, N. CHANG*, *Baylor College of Medicine, Houston, TX, **National Cancer Institute, National Institutes of Health, Bethesda, MD, ***Bionetics, Inc., Kensington, MD.

Human B-lymphotropic virus (HBLV), a new member of the herpesvirus family, has been recently detected in several patients with lymphoproliferative disease including the chronic mononucleosis fatigue syndrome. Several subgenomic fragments of HBLV have been molecularly cloned into bacterial plasmids and partially characterized. A combined cloning/expression protocol was used to identify a gene encoding a viral protein that is immunoreactive with sera from patients infected with HBLV. Random fragments were generated from the HBLV subgenomic DNA derived from pZVH14 by DNase Bal 31 digestion or sonication were inserted into an expression vector pMLB1111 and the HBLV DNA sequences were expressed as proteins fused to β-galactosidase. Several different open reading frames were mapped along the subgenomic DNA fragment. Sera from patients infected with HBLV were used to screen for HBLV immunoreactive fusion proteins. Two expression plasmids were isolated and their specific fusion proteins were identified with patient sera in the Western blot analysis. The HBLV DNA sequences represented in these two clones were mapped within a single open reading frame on the HBLV genome. Using affinity chromatography and SDS-PAGE, the HBLV-β-galactosidase fusion protein was purified and monoclonal antibodies were raised against them in mice.

TP.12 Western Blot Assay Patterns of Early Antibody Response to the Human Immunodeficiency Virus. Patricia E. Taylor, Cladd E. Stevens and Pablo Rubinstein, The New York Blood Center, New York, N.Y., U.S.A.

Stored serial serum samples from 103 homosexual men who participated in hepatitis B vaccine efficacy trials begun in late 1978 and who showed seroconversion during the subsequent 8 year period for antibody to the human immunodeficiency virus (anti-HIV) were tested by the enzyme-linked immunosorbent assay, ELISA, (Dupont Inc.). Sera obtained at and three to six months prior to anti-HIV positivity by ELISA were also examined by Western Blot (WB) procedure (Biotech Laboratories, Inc.). The WB patterns for 59 of these men showed anti-HIV reactivity for p24, p41 and other HIV proteins at the same time as ELISA reactivity was first observed. The remainder showed diverse patterns of early anti-HIV reactivity, the most common being anti-p24 reactivity with or without anti-p55. In 12 men anti-p24 was the first antibody to HIV to appear by WB. In five of these the ELISA result was negative when anti-p24 appeared and, in another, ELISA gave a positive reaction in a serum sample taken two months before the anti-p24 positive sample. The remaining seven were both ELISA and WB positive. The appearance of anti-p55 preceded anti-p24 and other antibodies in six instances. Anti-p41 was not found before the appearance of anti-p24 or anti-p55 or before antibody was detected by ELISA.

No relationship was found between the pattern of early anti-HIV response as observed by WB and the T helper to T suppressor cell ratio obtained in early 1984 when studies of cell-mediated immunity were initiated.

TP.13 Demonstration of Antigenic Variation in HIV Envelope Proteins by Competitive Radioimmunoassays.

J.W. BESS, JR.*, S.W. PYLE*, AND L.O. ARTHUR*, *Program Resources, Inc., NCI-Frederick Cancer Research Facility, Frederick, MD 21701, USA.

Competition radioimmunoassays have proven extremely useful not only in quantitation of biologicals but for establishing immunological relationships as well. We have purified the outer envelope glycoprotein (gp120) of HTLV-IIIB and used it in establishing competition radioimmunoassays. A broadly specific immunoassay was obtained when HTLV-IIIB gp120 was used as the radiolabeled probe in a competition assay with serum from an AIDS patient. All HIV variants tested in this assay competed completely with equal efficiency providing an assay for quantitating gp120 in viruses and other biological samples. Use of antisera generated against purified HTLV-IIIB to precipitate ^{125}-I HTLV-IIIB gp120 provided an immunoassay which differentiated HIV variants. HTLV-IIIB competed completely in the assay while the variant HTLV-IIIRF gave only partial competition. Use of these radioimmunoassays, along with an HTLV-IIIRF gp120 currently being developed, will provide rapid sensitive assays for establishing HIV envelope relatedness. This information, coupled with data from envelope nucleotide sequencing data and cross-neutralization results, will be potentially invaluable in assessing HIV isolates to be used in vaccine strategies.

Research sponsored, at least in part, by the National Cancer Institute, DHHS, under Contract Number NO1-CO-23910 with Program Resources, Inc.

TP.14 Topographical Analysis of HIV p24 using Monoclonal Antibodies

KEVIN J. REAGAN, A. L. PIEPER, M. A. WALSH and R. L. TYSON, E. I. Du Pont de Nemours and Co., Inc., Medical Products Department, Wilmington, DE 19898.

We have prepared panels of monoclonal antibodies reactive with the major internal core protein (p24) of Human Immunodeficiency Virus (HIV). Balb/c mice were immunized with partially purified virus or isolated viral proteins and immune splenocytes fused with variant 653 or P3x63 Ag8 mouse myeloma cells. Reactive hybridomas were initially screened on Du Pont HTLV-III ELISA plates. A further characterization of antibody specificity was accomplished by Western Blot reactivity with electrophoretically separated virus, surface and cytoplasmic immunofluorescence on virus-infected H9 cells and reactivity with recombinant core proteins.

Over 20 monoclonal antibodies specific for the p24 core protein were isolated and used to construct a functional epitope map. We identified four reactivity patterns representing three distinct antigenic sites on this protein.

TP.15 Complete Nucleotide Sequence of the Simian T-Lymphotropic Virus Type III and Genetic Analysis of a New Subgroup of AIDS-Related Human T-Lymphotropic Viruses

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A new primate retrovirus, simian T-lymphotropic virus type III (STLV-III), recently has been isolated from healthy African green monkeys and is apparently non-pathogenic in its natural host. However, spontaneous infection and inoculation of STLV-III into Macaque monkeys induce a disease like human AIDS. Independent isolates of human retroviruses related to STLV-III have been obtained from healthy individuals (HTLV-IV) and patients with AIDS ($LAV\text{-}2_{FG}$ and SBL-6669) from West Africa. We molecularly cloned the STLV-III genome and generated probes from the gag and envelope genes and determined genetic relatedness by Southern analysis of these simian and human retroviruses. Our results indicate that all these retroviruses are genetically closely related to each other. HTLV-IV and STLV-III genomes differed only in 2 of 15 restriction enzyme sites while $LAV\text{-}2_{FG}$ and SBL-6669 exhibited greater polymorphism as compared to HTLV-IV and STLV-III. Computer analysis of the nucleotide sequence obtained from the cloned STLV-III genome in comparison to that of HTLV-III showed a high degree of homology, suggesting common ancestry of these two viruses. Comparison within specific viral genes has allowed characterization of biologically important regions within the env gene and functional domains of some of the genes encoding regulatory proteins for the AIDS and AIDS related viruses.

TP.16 Phorbol 12-Myristate 13-Acetate Enhances HIV Promoted Gene Expression and Acts Upon a 12 Base Pair Functional Enhancer Element.

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Phorbol 12-myristate 13-acetate (PMA) is a potent inducer of T-cell immune functions and has recently been demonstrated to increase viral replication in cell lines infected with Human Immunodeficiency Virus (HIV). In order to define sequences required for viral induction by PMA, cell lines were transiently transfected with viral long terminal repeat (LTR) sequences directing chloramphenicol acetyl transferase (CAT) gene expression. 10 ng/ml PMA added to transfected cell cultures 24 hr before harvest reproducibly increased both CAT mRNA and enzyme expression 2 to 5 fold. Induction of CAT expression occurred in T-cell lines, monocyte lines, and cultured peripheral blood lymphocytes.

Sequences necessary for basal and PMA induced levels of CAT expression were determined by transfecting cells with deletion mutants constructed from the original LTR-CAT expression plasmid. Removal of U3 DNA 118 base pairs (bp) upstream of the mRNA start site improved basal and induced levels of CAT expression up to 5 and 50 fold, respectively. Deletion of DNA 68 bp upstream of the mRNA start site eliminated the basal expression level and prevented PMA induction. Basal and induced levels of CAT expression were restored by introducing a synthetic oligonucleotide containing a 12 bp LTR sequence. The enhancer-like sequence could be inserted at a site distal to the CAT gene open reading frame and functioned in a position and orientation independent manner. In summary, the data defines a transcriptionally active and PMA inducible regulatory/enhancer element critical to the control of HIV gene expression.

TP.17 Inhibition of HIV by Species of Recombinant Interferon Alpha

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It has previously been reported that recombinant interferon alpha-A has a dose-related suppressive effect on HIV replication in peripheral blood mononuclear cells in vitro. Based on this initial work, we investigated the effects of 6 species of recombinant human interferon alpha on HIV (HTLV-III B strain) infection of the T lymphocyte cell line H9 and the monocytoid cell line U-937. Both cell lines were mycoplasma free and maintained an RPMI 1640 with 20% fetal calf serum. Cultures were treated with either a single dose or multiple doses of recombinant interferons alpha A, A/D, C, K, I, or D at concentrations of 16, 256, and 1024 U/ml. Viral infection of target cells was quantitated by indirect immunofluorescence and reverse transcriptase (RT) activity in H9 on days 7 and 11 and in U937 on days 14 and 18. A dose response for HIV inhibition was seen with all species of alpha interferon. Single doses of interferons A, A/D, K, and I at 1024 U/ml completely inhibited HIV replication in both H9 and U937. Interferons alpha C and D were less inhibitory by 1-2 logs of RT activity. Approximately 50% inhibition of HIV infection was seen at 256 U/ml. Multiple doses of all six alpha interferon species were effective in U937 cells with total suppression seen with all species at 1024 U/ml. Cell viability was not impaired with interferon therapy; indeed, the survival of both H9 and U937 cells was improved by 10-25% in the presence of 256-1024 U/ml of interferon. These studies demonstrate that the interferon alpha family has antiretroviral activity in vitro in lymphoid and monocytoid cell systems and may be clinically useful in the therapy of AIDS.

TP.18 Synthetic peptide analogs of HIV proteins are recognised by naturally acquired antibodies.

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Predicted amino acid sequences of HIV proteins were scanned for potential antigenic epitopes using the Welling Antigenicity program (FEBS lett. 188, 215-9, 1985). Conserved, hydrophilic sequences identified were synthesized as 13-21mer peptides using automated Merrifield solid phase techniques. Peptides synthesized included gp120(2-13), gp120(55-65), gp41(582-596), gp41(579-600), gp41(659-670), gp41(766-778), ptat(60-72), and ptat(46-58).

Peptides were studied by ELISA for recognition by human antibodies. All peptides could be recognised, with sera from 98% of viraemic patients recognising gp41(579-600), and 73% of identical sera the truncated form (582-596). These results concur with those of Wang et al (PNAS, 83,6159-6163, 1986). Ptat(60-72) was recognised by 52% of sera from viraemic patients.

Serum from one viraemic patient with antibodies against core proteins only on immunoblot assay did not recognise any of the peptides. Individual profiles of recognition of peptides did not vary over time, but differed substantially between individuals .

These findings demonstrate the significance of natural variability of HIV isolates, and offer a means of further defining conserved, immunogenic epitopes for serodiagnosis or vaccine development.

TP.19 Chronic Infection of Non-human Primate Gibbon Ape (Hylobates lar) by Human Immunodeficiency Virus (HIV), $HTLV\text{-}III_B$.

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Many attempts have been made to identify animal model systems suitable for the study of pathogenesis resulting from infection by HIV and its prevention or treatment. To date, the persistent infection and immune response following inoculation with virus or tissues from AIDS patients had been documented in only one animal, i.e., chimpanzee (Pan troglodytes) (1,2). We describe here the extension of these observations to an additional non-human primate, the gibbon ape (Hylobates lar). The infection, recognized by isolation of infectious virus from peripheral blood mononuclear cells and appearance of specific antibodies, was detected within two weeks following i.v. inoculation with concentrated $HTLV\text{-}III_B$, and has persisted for several months. During this period of time, other than possible lymph node involvement, no noteworthy pathological symptoms were detected. In parallel experiments, animals from three other primate species, i.e., Rhesus monkey (Macaca mulatta), African green monkey (Cercopithecus aethiops), and common marmoset (Calithrix jacchus jacchus), gave no evidence of infection and only sporadic or transient immune response was observed.

1. Alter, H.J., Eichberg, J.W., Masur, H., et al., Lancet ii:549, 1984.

2. Francis, D.P., Feorino, P.M., Broderson, J.R., et al., Lancet ii:1276, 1984.

TP.20 A Possible Role for Epitopes other than CD4 in the Receptor Complex for (HIV).

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It was demonstrated that the receptor for HTLV-III on T-helper lymphocytes includes the CD4 protein complex. However, we have demonstrated that EBV genome positive B-lymphocytes can be infected by HTLV-III regardless of the presence of CD4 detectable by immunofluorescence of immunoprecipitation procedures. To further investigate these observations, monoclonal antibodies directed against multiple CD4 epitopes were used to compete with HTLV-III infection of two highly susceptible lymphoblastoid cell lines. This treatment failed to completely block HTLV-III infection of either CD4- or CD4+ B cell lines at concentrations that completely blocked the infection of CD4+ T-cells including fresh leukocytes from human peripheral blood and established T cell lines. B-cell specific monoclonal antibody (OKB-7) blocked EBV infection of B-cell lines but did not block infection by HTLV-III, suggesting that HTLV-III does not use the EBV receptor. These observations further auggest that CD4 proteins are not required for the infection of all susceptible target cells. However, the presence of these epitopes may constitute a high affinity receptor for HTLV-III. Concerning susceptable B-cells, EBV may code for or induce the synthesis of molecules that fulfill the receptor function.

TP.21 Immunological and Chemical Analysis of HTLV-III p15

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The first open reading frame of HTLV-III$_B$ genome has been identified as the gag gene. The proteins encoded by this gene are p17 as the amino terminal protein, p24 as the middle peptide and p15 as the carboxy terminal end. A monoclonal antibody recognizing p15, designated M35/2F8 has been developed and used to further characterize this protein. p15 was purified from an extract of H9 cells producing HTLV-III$_B$ by an immunoaffinity procedure employing immobilized purified M35/2F8 IgG. In addition to p15, M35/2F8 purified the precursor of gag proteins p53, a smaller intermediate p39, and at a lesser concentration a very small peptide of approximately 6 kD. In contrast, M35/2F8 purified only p6 when viral extract was applied to the immunoaffinity column. H9 cells producing HTLV-III$_B$ were then labeled with [^{35}S]-cysteine and [^{3}H]-leucine, immunoprecipitated with M35/2F8 and analyzed by SDS-PAGE. No immunoprecipitation of p6 has been observed when cells or virus were labeled with [^{35}S]-cysteine. However p6 was distinctly immunoprecipitated when [^{3}H]-leucine labeled cells were analyzed. These results demonstrated: that gag p15 is indeed processed into two smaller products p7 and p6 as anticipated, that M35/2F8 recognizes an epitope on the cysteine free peptide p6 and that p6 arises from a maturation cleavage of p15. To confirm its viral origin, [^{3}H]-leucine labeled p6 was subjected to radiolabel sequencing. Leucine was unambiguously assigned at position 1 and 13 of the 40 cycles examined. The amino acid sequence determined is a perfect match with a predicted sequence at the carboxy terminus of the gag gene starting with Leu^{448}.

TP.22 Interaction of Human Immunodeficiency Virus with Neural Cells Isolated from the Human Fetus Nervous System

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Human immunodeficiency virus (HIV), the primary etiological agent of acquired immunodeficiency syndrome (AIDS), has been implicated in the causation AIDS-associated neurological dysfunction and may be responsible for an increasing number of neonatal immunologic and neurologic disorders. However, as yet there is no model system available to investigate the interaction of HIV with the developing human nervous system *in vitro*. To examine the intracellular events associated with HIV infection of the human fetus nervous system we infected cells obtained by enzymatic dissociation of aborted human fetus dorsal root ganglia and their attached spinal roots and nerves. The expression of the HIV *gag* gene protein products (p17 and p24) was detected in a subpopulation of cells with a non-neuronal morphology, reaching a maximum within 3 days. Although 70% of the non-neuronal neural cells were p17- and p24-positive 3 days after infection, a majority of the cell population survived acute HIV infection, with the expression of p17 and p24 decreasing below the limit of detection by 12 days postinfection. Additional studies have demonstrated that the number of HIV-p17/24 nonneuronal neural cells detected 3 days postinfection decreased in direct correlation with increasing time of *in vitro* maintenance of the human fetus neural cells prior to HIV infection. These results suggest that *in vitro* maintenance of the neural cells after isolation from human fetus DRG and adjacent spinal root and peripheral nerves may result in plasma membrane alterations that interfere with HIV attachment and/or penetration or an intracellular physiological change that impairs at least the expression of the *gag* gene protein products p17 and p24 after infection or possibly a combination of both. This system may prove useful for examining the neuropathogenesis of HIV infection of the developing human nervous system.

TP.23 Glycosylation Inhibitors Block the Expression and Function of HIV Glycoproteins and Their Receptor(s)

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The interaction of envelope glycoproteins of HIV (gp110 and gp41) and their receptor(s) is responsible for viral entry and cell fusion; 2-deoxy-D-glucose (2-dGlc) blocks the expression of HIV glycoproteins. Uninfected MT-4 or CEM cells were treated with 5-10 mm 2DGlc for 24-96 hrs. One-half were infected with HTLV$_{3-B}$; an untreated group of cells were similarly infected. Fresh medium (with or without 2-dGlc) was added and the cells incubated for an additional 72 hrs. Triton X-100-lysed cells or glutaraldehyde-fixed cell surfaces were interacted with polyclonal antibodies against HIV-recombinant proteins (p ENV9, pENV14, pENV14, pENV120, pENV7). Alternatively, uninfected cells were interacted with monoclonal antibodies against T4, T4A, T8 and the IL-2 receptor. Bound antibodies were quantified with [^{125}I]-F(ab')2 fragments of antimouse IgG or [^{125}I]-antigoat IgG (rabbits). By trypan blue exclusion and light microscopy, 2-dGlc-treated cells were protected against CPE by HIV. Treatment of MT-4 cells with 2-dGlc produced a 35% decrease in the binding of OKT4A (to the putative receptor) vs controls. Using [^{3}H]-Ricin communis or gal oxidase technique with LI^{3}HB$_4$, we observed a 35-60% decrease in binding or labelling of gp41 or gp110 in dGlc-treated-cells; this was confirmed by P.A.G.E. or Western Blots. These studies support the view that glycosylation inhibitors block the initial steps of HIV-infection and should prove useful in the treatment of AIDS.

TP.24 Human Immunodeficiency Virus (HIV): Fine Structure and Immunolocalization of Virus Strucutral Proteins and HLA-Determinants.

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Thin section electron microscopy (EM), serial sectioning and tilting experiments were applied to elucidate the fine structure of HTLV-III B and LAV-2. On the envelope 70 - 80 knobs are observed having a diameter of 15, and a height of 9 nm. Knobs are arranged according to surface replica EM, in a T = 7l symmetry and are shed concomitant to the morphological maturation of HIV. Adjacent to the inner leaflet of the viral membrane an electron-dense matrix protein is seen which enlarges parallel to the long axis of the elongated prismatic viral core.

The antigenic architecture of the virion was investigated by pre-embedding immunoferritin EM and immunogold labeling of ultrathin cryosections. The core shell shows tubular symmetry and p24 antigenicity, while p17 determinants are associated with the matrix protein: both were not detectable on the outside of the virion. The major envelope gp120 forms the knobs and gp41 represents the transmembrane protein. HLA-antigens were shown to be incorporated in the envelope corresponding to the antigenic make-up of the virus-producing cell. Combining morphological and immunological observations a structural model of HIV is proposed.

TP.25 An Assay for HIV-p24 Antigen With Chemiluminescence Detection Using Antibodies Against Synthetic Oligo-Peptide Fragments of the Major Core Protein

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Antibodies against 2 separate epitopes of p24, the major core protein of the human immunodeficiency virus were obtained in sheep on immunisation with short synthetic oligopeptides. After purification by affinity chromatography, one antibody is coupled to polysterene beads as solid phase, the other to a diacyl hydrazide as chemiluminescence label. This Lumitest sandwich-type immunoassay requires a one-step incubation at room temperature overnight. The assay protocol includes pretreatement with sodium dodecyl sulfate for denaturation, thus minimizing risks in handling infectious material and reducing interference from human antibodies against p24, present in many sera, often leading to false results in other antigen assays.

In 9 out of 24 follow-ups of male homosexuals taking part in a prospective study, p24 antigen was detected up to 6 months prior to seroconversion. In serial samples of 1 additional patient who showed after seroconversion persistently very low antibody titers, p24 antigen was found always.

The assay can be used to determine LAV-2 in cell culture supernatants, too, as these antibodies are highly cross-reactive with the p24 protein of this variant.

TP.26 Inhibition of HIV reverse transcriptase activity by culture fluids from HIV-infected, Epstein-Barr virus-transformed cells.

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Most individuals who are infected by HIV are also sera-positive for Epstein-Barr virus (EBV) and it is important to understand potential relationships between these two viruses. We used EBV progeny from the simian B-95-8 cell line to infect and transform unstimulated cord blood lymphocytes. Following the establishment of EBV-transformed B cell lines, these cells were super-infected with the HTLV-III$_B$ strain of HIV. These cultures were examined periodically for viral reverse transcriptase activity, by means of a polyethylene glycol precipitation procedure, and for the presence of intra-cellular viral antigens, by an indirect immunofluorescence assay using mouse monoclonal antibodies against the HIV proteins p15 and p24 (kindly supplied by Dr. R.C. Gallo). By 17 days after infection about 15% of cells had become positive for HIV antigens, yet no RT activity could be detected in the culture fluids. To investigate this further, aliquots of viral pellets from the HIV-infected, EBV-transformed cells were mixed with equal volumes of similar material obtained from H-9 cells, continuously infected with HTLV-III$_B$. RT activity of the latter preparations was inhibited by 88% when the assays were performed immediately and by 95% if the samples were allowed to co-incubate for 3 hr at 37°C. These data suggest that EBV or EBV infection may have an inhibitory effect on HIV RT activity.

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TP.27 Kinetics of HIV infection after IV exposure to blood from an AIDS patients.

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A 40 year old man was contaminated by IV injection (10 ml) of an AIDS patient's blood, from which HIV had been isolated. He developed clinical symptoms of primary HIV infection 23 weeks later. His virological status follow up was assessed by ELISA , Western Blot (WB) and PBL cultures (PBLC).

	Weeks	PBLC	ELISA	WESTERN BLOT					
			+⩾0.30	18	25	41	55	110	160
	-40		- 0.036	-	-	-	-	-	-
IV 10 ml	→ 0								
	8	ND	- 0.016	-	-	-	-	-	-
	18	+	ND						
	19	+	ND						
Clinical symptoms→	23	+	- 0.133	+	+	-	-	-	+/-
	24	ND	- 0.103	+	+	-	+/-	-	+/-
	25	ND	- 0.221	+	+	-	+/-	-	+/-
	28	+	+ 0.49	+	+	-	+/-	-	+
	29	ND	+ 0.45	+	+	+/-	+/-	-	+
	32	ND	+ 0.58	+	+	+	+	+	+
	33	ND	+ 0.907						

Our data show after contamination : 1) positive PBLC at W18 ; 2) positive WB at the time of clinical symptoms (W23) ; 3) Positive ELISA at W28. On W33, the patient had nor ARC nor AIDS.

TP.28 A Rapid, Simple and Economical Screening Assay for Antibodies to the Human Immunodeficiency Virus (HIV).

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A dot enzyme immunoassay for the detection of anti-HIV antibodies was developed using an antigen derived from a recombinant HIV envelop protein, peptide 121 (Centocore, Inc., Malvern, PA). The assay can be performed in 30 minutes with a qualitative endpoint that does not require expensive instrumentation. Antigen was spotted onto opaque, high-impact polystyrene cards. The test was performed by adding human serum, plasma, lysed whole blood or saliva, alkaline phosphatase-conjugated goat anti-human IgG and substrate to the antigen spot with washing between reagents. A bright blue color developed on the antigen spot for positive specimens, and negative samples yielded no color. Correlations of results with western blot (WB) were as follows:

Specimens	Source	No. Tested/No. WB Positive	%Correlation
Serum/Plasma	USA	118/60	99.2
Serum/Plasma	Africa	103/50	98.6
Whole, lysed blood	USA	115/50	98.3
Saliva	USA	20/8	100

This assay may be useful for anti-HIV antibody screening for blood donors, epidemiologic studies or initial clinical assessment in remote areas of the world.

TP.29 Attempts to Produce a Progressive Immune Deficiency and Encephalopathy in Nonhuman Primates with the Human Immunodeficiency Viruses.

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Of the multiple nonhuman primate species we have investigated to date, including African green and marmoset monkeys, only chimpanzees (Pan troglodytes) and rhesus monkeys (Macaca mulatta) are susceptible to experimental infection with the human immunodeficiency viruses (HIV). Chimpanzees develop persistent infection following intravenous and/or intracerebral inoculation with strains of HIV, with brain tissues and plasma from AIDS patients, or with blood from experimentally infected chimpanzees. None of 24 HIV-infected chimpanzees monitored for nearly three years has developed a wasting illness, neoplasm or encephalopathy, despite persistent viremia. Signs of an immunodeficiency syndrome, as evidenced by opportunistic infections and abnormalities in T-cell subpopulations and in in vitro lymphoproliferative responses to mitogens, have not occurred. However, a chimpanzee, inoculated intravenously with whole blood from an HTLV-III$_B$ infected animal, has, on routine skin testing for tuberculosis, become tuberculin-reactive 23 months postinoculation. Mycobacterium avium-intracellulare was isolated from gastric washings, but no pulmonary or gastrointestinal focus of infection was found. The animal has developed inguinal lymphadenopathy, but is otherwise clinically well. This mycobacterial infection may represent the first indication of an underlying immunodeficiency, and studies to determine the extent of infection are underway.

TP.30 Synergism and Antagonism In Vitro Among Various Antiviral Drugs In the Treatment of HIV Infections.

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An effective therapy is urgently needed for individuals infected with the Human Immunodeficiency Virus (HIV). Combined therapy with two antiviral drugs that show in vitro or in vivo activity against HIV offer the potential benefits of enhanced antiviral activity, reduced toxicity and prevention of resistance.

We thus evaluated various combinations (Table) in vitro utilizing different cell culture systems including peripheral blood lymphocytes, H9 cells and a human monocyte line (BT4). HIV replication was assessed by reverse transcriptase activity, indirect immunofluorescence, p24 capture immunoassay and virus yield. Drug interactions were mathematically evaluated by the median effect principle and the isobologram technique.

Drug Combination		Effect
Phosphonoformate	+ Recombinant Interferon alpha A	Synergy
Azidothymidine	+ Recombinant Interferon alpha A	Synergy
Azidothymidine	+ Ribavirin	Antagonism
Azidothymidine	+ Lymphoblastoid Interferon	Synergy
Ribavirin	+ Phosphonoformate	Synergy

Ribavirin's antagonism of AZT resulted from phosphorylation inhibition. Other combinations are under study. Drug interactions should be considered when planning clinical trials of anti-HIV combinations.

TP.31 Regulation of mRNA Accumulation by a Human Immunodeficiency Virus Trans-Activator Protein.

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HIV LTR-directed expression is markedly stimulated in trans by coexpression of a region of the HIV genome encoding a portion of the tat reading frame. Transient expression assay analysis reveals that trans-activation of LTR-directed expression results primarily from an increase in mRNA accumulation. Deletion analysis of the LTR indicates that upstream enhancer elements are dispensible for trans-activation, while sequences 3' of the RNA start site displaying strict orientation and position dependence are required. These sequences, contained in the 5' leader of all HIV transcripts, form a stable stem-loop structure with twofold symmetry in the cognate mRNA. Analysis of mutations in the trans-acting region demonstrates that the trans-activator is the protein product of the tat gene. This protein has been identified biochemically in HIV-infected and transfected cells as an M_r 15,000 polypeptide. We discuss possible mechanisms whereby the interaction of p15tat with the dyad element promotes the accumulation of LTR-directed mRNA.

TP.32 Reactivity of HIV and LAV II Positive Sera with a Synthetic Peptide Antigen in the p34 Nuclease/Integrase Protein.

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A synthetic peptide antigen has been prepared which represents a conserved epitope in the 34kD (Nuclease/Integrase) protein present in HIV. The peptide designated 124 was tested for its reactivity with a panel of 46 sera (35 HIV positive and 11 HIV negative). As compared to the Genetic Systems whole virus assay (LAV-EIA) for detection of antibody to HIV, peptide 124 showed a specificity of 100% and a sensitivity of 97%. Peptide 124 was tested against an additional panel of sera of African origin. Of 61 African sera (28 positive, 25 negative, and 8 atypical by Western Blot), 96.4% (27/28) of positives, 0% (0/25) of negatives and 25% (2/8) of atypicals were positive. In addition, since peptide 124 represents a conserved antigenic epitope amongst AIDS viruses, we analyzed its reactivity with 10 sera that were characterized as positive for core and envelope antigens of LAV II by Western Blot. As expected, 100% (10/10) reacted in an EIA using LAV II as antigen, 70% (7/10) were positive with our standard LAV-EIA and 80% (8/10) using the single peptide 124 as antigen. These results are consistent with cross-reactions observed between the p34 proteins of HIV and LAV II in Western Blot analysis. In addition, no reactivity of peptide 124 was observed with HTLV I positive sera. These data indicate that peptide 124 will provide an additional tool in peptide based assays for HIV antibody detection.

TP.33 Replicative properties of transsectional and longitudinal HIV isolates from serum HIV-antigen positive and negative individuals

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Virus replication in co-cultures of lymphocytes of seropositive individuals and lymphocytes of healthy blood donors selected for susceptibility to HIV infection was quantitated by RT activity and a HIV p24 antigen capture assay. Virus was detected in 100% of AIDS and ARC patients (n=16), 84% of LAS patients (n=6) and 71% of asymptomatic individuals (n=38). Detection by antigen capture assay was considerably more rapid than by RT assay, especially in asymptomatics (mean: 14.0 vs. 28.1 days). HIV isolates obtained from lymphocytes collected over a two year follow-up period in six persons, showed similar culture characteristics within one individual. No clearcut differences were observed between serum HIV antigen-positive and -negative asymptomatic persons. Syncytia were detected in 40% of AIDS/ARC patients, 20% of LAS patients and 20% of asymptomatics. 8/9 Isolates that induced CPE in donor lymphocytes could be transmitted to H9, in contrast to 0/11 non-CPE inducing HIV isolates. One asymptomatic individual with in-vitro CPE-inducing HIV developed AIDS 16 months after first virus isolation. These data may imply that the probability of developing AIDS may be partly determined by the syncytium inducing capability of the HIV strain present in an infected individual.

TP.34 Comparisons of antigen detection and virus cultivation in HIV-1-infected patients

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All of 12 patients selected for an AZT-study gave before onset of treatment a positive HIV-1-result by lymphocyte co-cultivation in tissue culture. Using HIV-1-ELISA for antigen detection (duPont) 10 patients were significant reactive, 2 patients with ARC were negative. In HIV-1-infected children the ELISA-antigen-detection is independent from the amount of HIV-neutralizing antibodies. - The antigen ELISA shows a good sensitivity with a detection limit of 20 pg/ml serum. In comparison to a sensitive plaque titration assay on MT 4-cells one ng corresponds to $7x10^3$ PFU/ml.

TP.35 HIV tat/LTR-mediated Expression of Heterologous Genes in Transient Assays

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We have used transient expression assays to study the trans-activation of heterologous genes under the control of the HIV-IIIB LTR. Reporter genes included E. coli β-galactosidase, chloramphenicol acetyl transferase, and human IL-2. Expression of the reporter gene was monitored in cell lines from several species in the presence and absence of the following viral regulatory genes: HIV tat-III (under SV40 early transcriptional control), human CMV IE-1, pseudorabies virus IE, and human adenovirus-5 E1A. HIV tat efficiently induced LTR-mediated expression in HeLa cells (>400-fold) but was markedly less efficient in each of the nonhuman cell lines tested (2 to 30-fold induction). These results suggest that a major component of tat function is species specific. In HeLa cells expression of the reporter gene under tat-activated LTR control was 40-fold greater than the level expressed under SV40 early promoter control. CMV IE-1 significantly induced HIV LTR expression (~10-fold), whereas E1A had no effect on LTR expression. These results suggest that superinfection by CMV of a latently HIV-infected lymphocyte could result in activation of the HIV genome.

TP.36 Biologic and Molecular Characterization of Human Immunodeficiency Virus Isolated from Autopsied Brain of a Dementia Patient.

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To study the biologic and molecular nature of human immunodeficiency virus (HIV) infecting patients with neurologic disorders, we isolated HIV_{BR} from the autopsied brain tissue of a 57-year-old man who died of progressive dementing illness. Isolated virus was identified as HIV by antigenic crossreactivity and nucleic acid hybridization to HIV-specific antibodies and DNA probes. We studied the expression of viral proteins by immunoprecipitation analysis of infected cells. To further determine its biologic specificities, HIV_{BR}, was characterized for replication and extent of cytopathicity to $OKT4^+$ cells and compared with a standard HIV (HIV_{451}) isolate used in our laboratory. We observed that seven days after infection HIV_{BR} replicated 10-fold less than HIV_{451} but was essentially as cytopathic as HIV_{451} to $OKT4^+$ cells. We examined the genetic specificites of HIV_{BR} by molecularly cloning it and mapping it by restriction enzymes. The restriction enzyme sites, Sac I, Pvu II, Eco RV, Xho I, appeared conserved in the LTR of this neurologic isolate as in some of the previously reported HIV isolates, whereas some restriction enzyme sites, Bam HI, Ava I, Sal I, were not present throughout the genome. For detailed analysis of the conserved and variable domains of HIV_{BR}, we subcloned a 3.5 Kb fragment from 3' half of the genome encompassing env gene. The salient features of the nucleotide sequence analysis of HIV_{BR} with special reference to gp41 will be elaborated.

TP.37 HIV-1 and LAV-2/HIV-2 : serological cross-reactivities.

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A Human Immunodeficiency retrovirus named Lymphadenopathy-Associated-Virus type 2, LAV-2/HIV-2 was isolated in 1986 from two west african patients with AIDS. HIV-1 and HIV-2 exhibited cross-reactivity restricted to the gag and pol gene products. No cross reactivity was demonstrated between HIV-1 (gp110, gp41 and their precursor gp160) and HIV-2 (gp130-105, gp41-36) envelope glycoproteins. HIV-2 antibodies were detected by Elisa using HIV-2 purified viral antigen prepared from the CEM-infected cell line and control antigen. The diagnosis of HIV-2 infection was demonstrated by the presence of antibodies to the HIV-2 glycoproteins by Western Blot analysis. HIV-1 antibodies were detected by Elavia and LAV Blot (Diagnostics Pasteur). 41 HIV-2 positive sera were studied by HIV-1 Elavia : 18/41 sera were completely negative : 10/13 collected from AIDS patients, 7/25 from asymptomatic subjects (AS) and 1/3 from ARC. 179 HIV-1 positive sera were tested by HIV-2 Elisa. 37/179 (21%) were positive or border line : 3/42 from AIDS patients, 20/63 from ARC and 14/74 from AS. In AS, 81% of HIV-1 positive sera were negative by HIV-2 Elisa whereas 28% of HIV-2 positive sera were negative by HIV-1 Elisa ($p < 10^{-9}$). Moreover these data demonstrated that cross-reactivity between HIV-1 and HIV-2 does not allow to pick up HIV-2 seropositivity using HIV-1 Elisa in HIV-2 AIDS patients (76% HIV-1 negative) as in HIV-2 AS (28% HIV-1 negative). Specific HIV-2 assays are needed to screen blood donations as to perform HIV-2 seroepidemiological surveys.

TP.38 Virologic Endpoints in Antiretroviral Chemotherapy Trails

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Virologic measures may provide useful adjuncts to clinical or immunologic endpoints to assess the efficacy of chemotherapeutic agents in antiretroviral trials. Such nonclinical endpoints may be especially important in asymptomatic or mildly symptomatic patients where clinical endpoints are infrequent or will require prolonged observation. Two independent virologic measures, virus recovery from peripheral blood leukocytes (PBL) and p24 antigen detection in plasma or serum, have now been evaluated in placebo-controlled trials of 3'-Azido-3'-deoxythymidine (AZT) and Ribavirin which involved a total of 72 patients. Virus recovery was positive 92% of the total sample; detection of virus in cultures of PBL's by a supernatant p24 antigen radioimmunoassay (RIA) varied inversely with the absolute T4 lymphocyte count. Higher levels of T4 lymphocytes were associated with longer time required for detection of p24 in supernatant fluids. Direct testing of p24 antigen in serum was positive in 15/34 (44%) LAS patients, 10/26 (69%) ARC patients and 10/12 (63%) AIDS patients suggesting a correlation of p24 antigen positively with both clinical state and T4 counts. In addition p24 antigen was inversely correlated to the level of p24 antibody measured either by a competitive ELISA assay using rDNA antigen or ^{125}I-virion p24 RIA. Treatment with AZT produced significant diminution in virus recovery within one month of treatment and there was a concomitant and significant decline in p24 antigen levels in patients receiving AZT, but not placebo patients. The correlation of these laboratory endpoints with clinical endpoints suggests that they will be useful surrogates for efficacy studies in future antiretroviral drug trials.

TP.39 **NEUTRALIZING ANTIBODIES IN HUMAN SERA BIND TO GENETICALLY ENGINEERED NON-GLYCOSYLATED GP120 PRODUCED IN YEAST.** K. STEIMER J. STEPHANS, M. SHUH and E. MILLER. Chiron Corporation, Emeryville, California, U.S.A.

Affinity columns of non-glycosylated genetically engineered polypeptides produced in yeast from defined regions of the HIV-SF2 envelope gene were used to fractionate HIV antibody-positive sera. Pooled sera from nine HIV seropositive blood donors were fractionated on these columns and the affinity purified antibodies were tested for neutralization of HIV-SF2. No neutralizing activity bound to env-5, a polypeptide in the amino terminal one-third of gp41, composed of amino acids 557-677 of the env gene product. In contrast, env-2, a recombinant polypeptide corresponding to amino acids 28-491 of env, bound a significant proportion of the neutralizing activity in this serum pool. There were also neutralizing antibodies that did not bind to columns of env-2. When env-2-specific antibodies were fractionated on columns of env-1, a polypeptide representing amino acids 28-277 of env, the majority of the neutralizing activity did not bind. However, there was some neutralizing activity in the env-1-specific antibody fraction demonstrating that antibodies able to neutralize HIV-SF2 can be specific for epitopes in the amino-terminal half of gp120. However, this activity represented only a minor fraction of the total env-2-specific neutralizing antibodies. When the sera from the pool were fractionated individually on env-2 columns, all showed evidence of env-2 specific neutralizing antibodies. We are currently assaying env-2 specific antibodies for neutralization of other HIV isolates and attempting to identify the target antigens for unbound HIV neutralizing antibodies.

TP.40 Prevalence, Incidence and Risk Factors of HIV-infection among Drug Addicts in Amsterdam

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In December 1985 an epidemiological study among drug addicts in Amsterdam was initiated. Recruitment takes place at methadone posts and the STD-clinic for drug using prostitutes. As of 15th October 1986, 243 drug users had entered the study of whom 80% were IV users. Prostitution was reported by 88% of 125 women and 20% of 118 men. Female prostitutes practised mainly vaginal and oro-genital intercourse and 91% reported frequent use of condoms. Male prostitutes practised mainly oro-genital and manual contact. At entry into the study 66/243 (27%) were anti-HIV seropositive; 64/66 were IV users and 2/66 male homosexuals. Antibodies to HTLV-I were found in 4/243 (1.6%), HBV-markers in 173/243 (73%) and syphilis markers in 21/243 (9%). HIV-seropositives reported significantly more often enlarged lymphnodes, coughing and herpes zoster. Risk factors significantly associated with HIV-seropositivity were: duration of IV drug use, frequent sharing of needles/syringes, West-German nationality and smoking of heroin ("protective"). No association was found with sex, age, prostitution and methadone use. Significant changes in lifestyle were found among participants towards a less risky behaviour (smaller proportion reporting daily IV use and using often the same needle/syringe; increasing proportion using needle/syringe exchange programme). However, among 50 HIV-seronegatives followed up, 4 HIV-seroconversions have (attack-rate 15% after 240 days), indicating that till now the prevention measures taken in Amsterdam have had only a limited influence on the speed with which HIV spreads among the drug users.

TP.41 Prevalences of HIV Antibodies and PGL in Rural Kenya

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A newly developed method, which is able to detect HIV antibodies in whole blood spots on filter-papers in both the ELISA and the immunoblotting test, was used to screen 603 Kenyans for the presence of HIV antibodies. By comparative testing of serum and whole blood filter-papers from 55 Kenyans and 15 Danes, the method was found reliable. The majority of the Kenyans were residents of a province in West Africa, while the rest were students from predominantly rural areas in other parts of Kenya. Median age was 18 years (range 0-70). Clinical examination was performed in 348 individuals.

Only 1 of the examined Kenyans had antibodies to HIV by both ELISA and immunoblotting, representing a prevalence of 0.17% (95% confidence limits: 0.00-0.93%). PGL was found in 25% of healthy adults, 90% of healthy children, 34% of non-venereal out-patients 22% of venereal out-patients, 21% of adult in-patients, and 50% of children in-patients, representing a 44% over-all prevalence of PGL.

Neither the low prevalence of HIV antibodies nor the high prevalence of PGL not associated with HIV infection is in accordance with results previously presented from rural districts in Kenya.

TP.42 An Old Disease Meets a New Disease: Tuberculosis and the Acquired Immunodeficiency Syndrome in New York City

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New York City (NYC) reported 1,843 tuberculosis (TB) cases in 1985, a 16% increase over the average annual number of 1,583 cases reported from 1979 through 1984. This included increases of 32% in blacks and 19% in Hispanics, groups with an increased incidence of the acquired immunodeficiency syndrome (AIDS). To determine if the increase in TB was AIDS-related, we matched the NYC TB and AIDS registries. The 266 patients common to both registries (TB/AIDS patients) comprised 2.3% of the 11,640 TB patients reported from 1979 through 1985, and 4.8% of the 5,545 AIDS patients diagnosed from 1981 through 1985. The TB/AIDS patients included 230 (86%) men and 36 (14%) women; 49 (18%) whites, 140 (53%) blacks, and 77 (29%) Hispanics; 81 (30%) homosexual or bisexual men, 132 (50%) intravenous drug abusers (IVDAs), 22 (8%) patients with both risk factors, and 31 (12%) persons with other risks for AIDS. In 175 (66%) the two diagnoses were made within a six month time span. Compared to TB patients without AIDS, TB/AIDS patients were more likely to have extra-pulmonary TB (46% vs. 20%, p<.001), two or more disease sites (25% vs. 4%, p<.001), a negative tuberculin skin test (26% vs. 7%, p<.001), and were less likely to have cavitary disease on chest radiograph (8% vs. 24%, p<.001). Compared to AIDS patients without TB, TB/AIDS patients were more often black (53% vs. 30%, p<.001), Hispanic (29% vs. 23%, p<.05), and IVDAs (50% vs. 28%, p<.001). These data suggest that AIDS is responsible for some of the increase in TB in NYC, that certain presentations of TB are associated with an enhanced risk for AIDS, and that some AIDS patients are at higher risk for TB.

TP.43 Natural History of HIV Infection in Spouses of AIDS Patients

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332 spouses/regular sex partners (M=53, F=279) of AIDS patients have been followed at our clinic in Port-au-Prince, Haiti since September 1983. Seropositivity for HIV (wv, p24, gp120) was 53% for females (n=148) and 55% for males (n=29) at the time of their initial visit. Ten percent of seropositive (SP) males and 12% of SP females had either AIDS or ARC on study entry. The seropositive asymptomatic female spouses were followed for a mean period of 15 months and male spouses were followed for a mean of 17 months (range 2-36 months for both groups).

The proportion of those followed who developed either AIDS or ARC was calculated using the Kaplan-Meier survival method. The percentages of initially asymptomatic seropositive females with either AIDS or ARC at 3, 6, 12 and 24 months of follow-up were 3, 5, 10 and 26%, respectively. The percentages of HIV-seropositive males with either AIDS or ARC at 3, 6, 12 and 24 months were 4, 13, 19 and 27%, respectively. Forty percent of the SP males and 25% of the SP females who developed either AIDS or ARC died within 24 months of entry. In addition, during a mean follow-up period of 14 months four initially seronegative asymptomatic spouses (3F, 1M) developed either AIDS or ARC.

To date, 8/29 (28%) SP male spouses and 34/148 (23%) SP female spouses have developed either AIDS or ARC. Asymptomatic SP spouses have developed either AIDS or ARC at a continuous rate of 1% per month over a calculated two year follow-up period.

TP.44 AIDS-Related Immune Thrombocytopenia: HIV Expression and Progression to AIDS.

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Thirty-five seropositive homosexual men with isolated immune thrombocytopenia (ITP) at initial presentation were diagnosed between 1982 and 1984. Their mean T-helper cell number was 390/mm3. Attempts to isolate HIV from 13 patients (pts) yielded positive results in only 2 cases. This rate of culture positivity (15%) is significantly lower than the 50% yield in healthy seropositives and the 75%-90% culture positivity seen in pts with AIDS and ARC employing identical cell culture techniques (Levy and Shinabukuro, J. Inf.Dis. 152:734, 1985). One positive pt was treated with prednisone and danazol but had been off therapy for 2 yrs at the time of culture. The other pt was virus positive at initial presentation in 1984 and remains stable with ITP without therapy. Three culture negative patients developed AIDS. Of the entire 35 member initial ITP cohort, ten pts (28.5%) have progressed to AIDS at a mean of 30 months (range 16-44) after ITP diagnosis. Five have expired. Spontaneous normalization of platelet count in the absence of therapeutic intervention antedated the AIDS diagnosis in 5 of 10 evolving pts. These data demonstrate an unusually low prevalence of infectious virus expression in this HIV-infected pt population compared to others; this finding does not appear to influence the progression to frank AIDS.

TP.45 Anti-HIV and Hepatitis B Markers in Canadian Volunteer Blood Donors.

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This study was undertaken to compare the association of exposure to Human Immunodeficiency Virus (HIV) with that of Hepatitis B Virus (HBV) in a population of volunteer blood donors. Sera from donors confirmed positive for anti-HIV by Western blot, negative for anti-HIV, and those confirmed positive for HBsAg (hepatitis B surface antigen) by neutralization with specific antibody were examined.

Comparison of the results for the anti-HIV positive and negative donors indicate a greater prevalence of HBsAg in the anti-HIV positive donor population than in the anti-HIV negative population.

Although anti-HIV testing was not initiated until November 1985, it was possible retrospectively to determine the anti-HIV status in HBsAg positive donors identified in 1985. The prevalence of anti-HIV in HBsAg positive donors was higher in 1986 than in 1985, but the difference was not significant ($p < 0.05$).

The observations of this study may indicate a trend towards a positive significant correlation of anti-HIV in HBsAg positive donors. If HIV infections increase as predicted, our results might indicate that the prevalence of HBsAg will also increase.

TP.46 **Understanding the Natural History of AIDS in West-Germany.A Prospective Study in Homosexual Men.**

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Seventyfive percent of AIDS patients in West-Germany are homosexual men.In 1984,93 gay men in Munich were enrolled in a prospective longitudinal study to investigate their seroepidemiological development in a combined biological and psychosocial approach.Besides medical history and physical exam virological, immunological and chemical lab data were obtained as well as data on sexual activity and psychosocial variables. Participants were followed for two years and classified using the Walter Reed staging classification for HIV infections.Seroconversion rate during the study period was 13%.HIV antibody positivity rose from 23% in 1984 to 33% in 1987.Three percent of the originally healthy homosexual men died from AIDS during the study period.Two thirds of HIV AB positive men showed signs of progressive illness.Early enlarged lymphnodes were correlated with relatively better prognosis.Condom use went up significantly.Saver sex behaviour characterised by protected anal intercourse or no anal intercourse was implemented to a significant degree whereas no significant change was seen for oral sexual activity.Anonymous sexual contacts decreased considerably. Sexual satisfaction as measured by a standardized test did not change with safer sex practices.

TP.47 Validation of AIDS Surveillance Through a One-Year Death Certificate Review.

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Previous validation studies using mortality data to evaluate AIDS surveillance have been of limited duration, and have found variable estimates of the completeness of reporting. To more precisely characterize the accuracy of Massachusetts surveillance, all 9432 death certificates issued in Boston, between July 1985 and June 1986 were reviewed manually. We evaluated 654 questionable cases including 128 with specific AIDS-related causes of death, 98 due to non-Hodgkin's lymphoma (NHL) or unspecified pneumonia (UP), and 428 other non-accidental deaths of males aged 20-50. Follow-up of 479 cases (73%) revealed obvious non-AIDS causes and 96 (15%) matched reported AIDS cases among 564 in the Massachusetts registry. The remaining 79 suspicious cases were investigated through their attending physicians and 61 (75%) were not considered to have human immunodeficiency virus (HIV) infection. The 18 HIV-related deaths included 11 AIDS cases which should have been reported, 2 diagnosed and reported in other states, and 5 which failed to fulfill the case definition. Causes of death listed for the 107 Massachusetts AIDS cases included AIDS (48%), P. carinii pneumonia (28%), UP (14%), Kaposi's sarcoma (13%) and NHL (6%). AIDS case reporting was 90% complete during this year.

TP.48 Retroviral Epidemiology in Jamaica, West Indies: the Introduction of HIV into an HTLV-I Endemic Island.

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Jamaica has a low incidence of AIDS (11 reported cases thus far on an island of 2 million) despite much trade and travel with the U.S.A. We therefore decided to investigate HIV seroprevalence in several large cohorts assembled for our studies of HTLV-I epidemiology. Sera that had been stored at -80 C were tested for antibodies to HIV using an ELISA assay (ENI). Reactive sera were confirmed by P24 and GP120 radioimmunoassays or by Western Blot. None of 4000 healthy food service workers were seropositive. This cohort is most representative of the general population, and has an HTLV-I seroprevalence of 5.8 %. Three of 2400 patients from two sexually-transmitted disease clinics were HIV seropositive; the clinic located in the tourist area did not have a higher prevalence. Of 125 homosexual and bisexual men, 10 % had anti-HIV antibodies, and sexual contact with Americans rather than promiscuity per se appeared to be associated with increased risk of infection. 10 % of the same cohort were HTLV-I positive, but only one man was seropositive for both viruses.

In conclusion, HIV seroprevalence is low in Jamaica, which is consistent with the low number of reported cases of AIDS. HTLV-I infection is endemic in Jamaica, while HIV has a very limited epidemiologic pattern suggesting limited introduction into groups having sexual contact with Americans. Surveillance of the local high-risk groups, combined with education, may help to limit introduction. Finally, medical evaluation of the high-risk groups will also provide valuable data on the consequences of infection with both retroviruses.

TP.49 Projections of AIDS Morbidity and Mortality in San Francisco.

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We projected AIDS cases and deaths in San Francisco for 1987 and 1988. Cases were projected by fitting Box-Jenkins time-series models to the epidemic curve for San Francisco. AIDS mortality was projected by applying Kaplan-Meier survival time estimates obtained from surveillance data to the actual and projected numbers of cases diagnosed per month. We predict that 1144 and 1222 new AIDS cases will be diagnosed in 1987 and 1988, respectively. The cumulative number of cases predicted through the end of 1987 and 1988 is 3879 (95% C.I. = 3236 - 4521) and 5101 (95% C.I. = 3686 - 6516), respectively, representing a doubling time of 26 months for the period beginning November, 1986 and ending December, 1988. A cumulative total of 2529 deaths are projected through December, 1987 (95% C.I. = 2256 - 2779), with 3552 deaths projected through December, 1988 (95% C.I. = 2854 - 4242). The proportion of cases among non-whites is expected to increase from 13.8% at present to 14.6% by the end of 1988, while the combined proportion of cases attributed to heterosexual IV drug use and to heterosexual contact is projected to increase from 1.6% to 2.0%. These projections suggest that the number of cases diagnosed by month will continue to increase through 1988, but that the rate of increase will be slower than that for previous years. The distribution of cases is expected to shift slightly, with an increase in the proportion of non-white, IV drug user, and heterosexual contact cases.

TP.50 The Descriptive Epidemiology of HIV Infection in the U.S. Army.

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In October 1985, as part of a comprehensive program to control the impact of HIV infections on military readiness, the Department of Defense (DOD) ordered the testing of all 2.1 million members of the Armed Forces. Under the current timetable the U.S. Army will complete screening of it's 764,000 active duty soldiers during the summer of 1987. The DOD defines HIV positivity as two positive ELISA tests confirmed by positive Western Blot assay of the initial and a subsequent specimen. Preliminary data on 135,412 soldiers tested between October 1985 and September 1986 indicate an overall HIV positivity rate of 0.98/1000. The prevalence among 19,446 officers tested is 0.51/1000; among 115,966 enlisted the rate is 1.06/1000. Prevalence rates are 1.01/1000 for males and 0.73/1000 for females. Rates by age are 0.23/1000 for those <20 years, 0.89/1000 for those 20-24, 1.35/1000 for those 25-29, 1.33/1000 for those 30-34, and 0.67/1000 for those 35 and older. Prevalences by race/ethnic group are 0.44/1000 for whites, 2.19/1000 for blacks, 2.12/1000 for Hispanics, and 0.95/1000 for other groups. Rates by marital status are 0.60/1000 for married soldiers, 1.46/1000 for those single, and 1.22/1000 for those no longer married. Updated figures on an estimated 500,000 tested soldiers will be presented along with data on HIV positivity by military occupation as well as home and assignment location.

TP.51 AIDS and the Potential for HIV Transmission in Minority Populations in San Francisco. GEORGE W. RUTHERFORD, GF Lemp, JL Barnhart, PE Evans, GA Bolan, D Werdegar, Department of Public Health, San Francisco, California.

To evaluate the current and potential impact of AIDS on minority communities in San Francisco, we analyzed AIDS and venereal disease surveillance data by race. Of the 2,760 cases of AIDS reported through December 31, 1986, 378 (14%) were in Blacks, Hispanics, and Asians. The incidence of AIDS among nonwhites, 1.21 cases per 1,000, was significantly lower than the incidence among whites, 6.59 per 1,000; and the incidence among Asians, 0.24 per 1,000, was significantly lower than among Blacks, 1.9 per 1,000, or Hispanics, 2.17 per 1,000. Of the 378 nonwhite AIDS cases, 332 (88%) were in homosexual or bisexual men. These men were more likely to be bisexual and to live outside "gay" neighborhoods than white homosexual and bisexual men. The proportion AIDS cases involving heterosexuals was significantly higher in nonwhites (9%) than in Whites (1%). Nonwhites constituted 67% of heterosexual intravenous drug users, 64% of heterosexual contact cases, and 44% of women and 57% of children with AIDS. Additionally, the annual incidences of syphilis and gonorrhea among women were significantly higher among Blacks and Hispanics than among White and Asian women with the highest incidences in the 15-19 and 20-24 year old age groups. We conclude that adolescent and young adult Black and Hispanic heterosexuals may be at significant risk for HIV infection in San Francisco.

TP.52 HIV infections in the People's Republic of Congo

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HIV-1 prevalence was investigated in different sub-population groups in 1985-1986. Among 50 patients suspected of AIDS in the General Hospital of Brazzaville, 28 (56%)were positive after confirmation by western blot in HIV-1 and 5 further had restrictive reactivities to gag gene products. The mean age was 24 years of age for both males and females. The prevalence rate in 1985 among 106 asymptomatic patients in the General Hospital in Brazzaville was 7.7 %, close to that observed in Zaire, in the general population.

In patients from neurology, oncology and infectious disease wards, but lacking signs of AIDS, the prevalence rates were respectively 9, 4 and 8 %. In the Public Health National Laboratory, Brazzaville, where patients are coming for sterility problems, 16.6 % were found to have antibodies to HIV-1. Possibly of greater interest was the comparison between 1985 and 1986 regarding pregnant women coming to the Public Health National Laboratory for screening of antibodies to German measles, toxoplasmosis and syphilis. In mid 1985, the prevalence rate of HIV antibodies in this group was 11 %, while in March-April 1986 18 % were positive. Such a progression of HIV-1 antibody prevalence among pregnant women raises a critical issue for newborns in epidemic aras. A longitudinal study of the positive pregnant mothers and offsprings is being implemented in Brazzaville, at the Public Health National Laboratory.

TP.53 Three-year progression to clinical AIDS in seropositive men: the San Francisco General Hospital Study.
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We examined progression to AIDS in 291 seropositive men first seen in 1983-84. 41/291 have progressed (14%) with median followup of 30 months. 13/41 were first diagnosed with Kaposi's Sarcoma (KS),2 with lymphoma, and 26 with OI and/or KS. Actuarial progression rates were 6% at 12 months, 12% at 24 months, and 24% at 36 months. There was no evidence of a declining progression rate.KS as a first diagnosis has become rare: 11/22 men progressing in the first 18 months were KS first diagnoses but only 2/19 progressing in the second 18 months.

Rate of progression was strongly associated with abs. no. and proportion of T4(helper) cells. 56% of men with 0-200 cells/cu.mm progressed vs. 23% of those with 201-400 cells and 9% of those with 400+ cells. Progression was also associated with no. of T lymphocytes and T8(suppressor) cells, Red blood count(RBC), hematocrit, hemoglobin level, sed. rate amd beta 2 microglobulin level at baseline but not with lymphadenopathy. In a multivariate analysis, no. of T4 cells, T4/T8 ratio and RBC were independently associated with progression. Hepatitis B carriers (HBsag+) were protected, 1/28 carriers progressing (3%) vs. 40/257 (16%) of those HBsag+ (p=.06).

There was a continuous loss in T4 cell population in men not progressing to AIDS. The percentages with 0-200,201-400 and 400+ cells going from 6%, 19% and 75% respectively at baseline to 11%, 26% and 63% at two-year clinical followup. Applying the multivariate predictor to the distribution of laboratory values at 2-year followup,the expected proportion progressing to AIDS in 5 years is 30-35%

TP.54 The Geographic Distribution of Human Immunodeficiency Virus (HIV) Antibodies in Parenteral Drug Abusers (PDAs)
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Opioid dependence treatment programs in 5 regions of the US collaborated in a study aimed at monitoring trends in seroprevalence of HIV antibodies. After informed consent, 1,650 PDAs volunteered to provide blood specimens and data on health history and patterns of drug use. While this sample cannot purport to be representative of PDAs in the region, nor even of PDAs in treatment within the region, the wide disparities in HIV seroprevalence in the face of similarities in drug using behavior have important implications for prevention. In the New York area (Harlem, Brooklyn), 61% of samples (N=280) obtained in late 1986 were positive, up from 50% of samples (N=585) from the same program taken in early 1984. In Baltimore, 29% of samples (N=184) representing 11 programs were positive. Significant sex and ethnic group differences were apparent. In contrast, samples from programs distant from the Northeast corridor had far lower rates: San Antonio, 2% (N=106); Tampa, 0%; Southern California, 1.5% (N=413, with samples from programs from Fresno to San Diego). Contrary to expectations, there was no corresponding difference in lifetime needle sharing experiences, which ranged from a low of 70% in New York to 99% in San Antonio. Because needle sharing is practiced by PDAs in areas where seroprevalence is still relatively low, these areas are vulnerable to the same catastrophic spread seen in the Northeast. But a window of opportunity where prompt, vigorous, and aggressive efforts at prevention could have major impact.

TP.55 Human Immunodeficiency Virus (HIV) Infection During Pregnancy: A Longitudinal Study.
THE NEW YORK CITY COLLABORATIVE STUDY GROUP FOR VERTICAL TRANSMISSION OF HIV. (SHARON NACHMAN, Lincoln Hospital/New York Medical College, New York, NY)

Over the past eight months pregnant women were prospectively enrolled to study the effects of HIV infection on pregnancy. Of 71 women enrolled known risk categories included IVDA 60%, sexual partners of IVDA 17%, both 9%, and one other. 44% were HIV positive, 44% HIV negative and 12% pending.

Both groups (seropositive and seronegative) were identical for race, age, income and education. Although a history of prior miscarriages was present in 33%, there were no differences in the two groups. The rates of pregnancy-related complications, i.e., hypertension, gestational diabetes, bleeding, concomitant infections and hospitalizations were also similar.

Only three women showed class III or greater HIV infection. None of the others showed signs of HIV related illness, and none developed them during pregnancy. There were no seroconversions in either group.

The immunologic profiles for the seropositive and seronegative groups were as follows: Initial IgG (X): 1700 mg/dl vs 1096 mg/dl; T helper cells: 719/cmm vs 1107/cmm; T suppressor cells: 721/cmm vs 710/cmm; and T4/T8 ratio: 1.0 vs 1.6. At delivery: IgG (X): 1430 mg/dl vs 1114 mg/dl; T helper cells: 796/cmm vs 1172/cmm; T suppressor cells: 839/cmm vs 970/cmm; and T4/T8 ratio: 0.9 vs 1.2. An unexpected finding was the depression of T helper cells in mothers using methadone only (X=358/cmm for seropositives, and X=804/cmm for seronegatives).

Our study shows there are no significant differences between the two groups with respect to history, obstetric history, and physical findings, and there is no progression of illness during pregnancy.

TP.56 AIDS Incidence in Pregnant Women, Their Babies, Homosexual Men and Hemophiliacs. JAMES J. GOEDERT*, S.H. LANDESMAN**, M.E. EYSTER***, R.J. BIGGAR*, *National Cancer Institute, Bethesda MD, **SUNY Health Science Center, Brooklyn NY, ***Penn State University College of Medicine, Hershey PA.

Crude and actuarial incidence of AIDS among human immunodeficiency virus infected (HIV+) subjects was calculated for two new cohorts (pregnant women and their babies), with 18-months additional follow-up for cohorts of hemophiliacs in Hershey PA and homosexual men in Manhattan NY and Washington DC described previously (Science 1986;231:992-5). Among 35 HIV+ second/third trimester pregnant women, none has developed AIDS but median follow-up is only 7 months, maximum 16 months. Among the 32 babies thus far born to these women, 2 (6%) have developed histologically proven Pneumocystis carinii pneumonia, 1 of whom died with cytomegalovirus colitis. Actuarial incidence of pediatric AIDS has been 8%±7% (SE) at age 7 months and 19%±13% at age 10 months (median follow-up 5 months, maximum 15 months). Among the prevalent (1982) HIV+ cohorts, there have been 2 new AIDS cases in Hershey hemophiliacs (7/50, 14% as of January 1987), 4 in NY homosexuals (17/43, 40%), and 7 in DC homosexuals (13/42, 31%). Out of 91 hemophiliacs (follow-up 6-112 months, median 56 months) there have been 10 AIDS cases 24-94 months after HIV seroconversion, for actuarial AIDS incidence rates of 5%±3% at 42 months and 24%±9% at 7.8 years after seroconversion. Among 43 seroconverters in the combined homosexual cohorts there have been 3 cases after 28-42 months, for an actuarial AIDS incidence of 10%±8% 42 months after HIV seroconversion. These are the best incidence data available to date and suggest: 1) that pregnant women must be evaluated further for AIDS risk; 2) that HIV+ AIDS-free survivors can be anticipated 9 years (>108 months) after HIV seroconversion; 3) that AIDS incidence after seroconversion may be slightly higher in homosexual men than in hemophiliacs; and 4) that the 1-year morbidity and mortality from pediatric AIDS will be high.

TP.57 Retrospective Case Study of Presumptively Diagnosed AIDS (PDA) in New Jersey

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Many patients with HIV infection do not meet CDC criteria for AIDS and are not counted in AIDS statistics, but they are presumptively diagnosed as having AIDS nonetheless. The NJSDH, in cooperation with CDC, conducted a retrospective study of 207 patients randomly chosen from the New Jersey registry who were entered into the registry between July 1985 and June 1986. All but three of the 207 had engaged in a known risk activity. The goal was to determine how many of these patients could, on closer examination, be shown to have AIDS.

Ten (5%) were diagnosed as meeting CDC criteria for AIDS; another 31 (15%) were PDA on the basis of physician opinion; and 99 (48%) met NJSDH criteria for ARC. Forty four patients (21% of the sample) had expired by the end of the period studied. Of the deceased, only one had been autopsied and met CDC criteria for AIDS. Another 17 (39% of the deceased) were judged PDA.

While the study suggests that the number of AIDS cases in New Jersey has been undercounted, more conclusive results would depend on more frequent autopsies of deceased PDA and more frequent attempts to make reliable diagnoses of living PDA.

TP.58

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

TP.59 Modeling the Spread of Human Immunodeficiency Virus (HIV) in the United States

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Despite widespread interest in the processes by which HIV infection has spread in various U.S. populations, there have been few attempts to develop mathematical models of the dynamics involved. Yet such models may be extremely useful in predicting the future course of the epidemic for health services planning purposes, identifying the most promising strategies for primary prevention, and estimating the aggregate effects of new medical interventions that are capable of lengthening individual survival. We have developed a computer model of the dynamics of HIV infection that takes into account a broad array of data on the size and sociodemographic composition of various risk groups, estimated seroprevalence rates, the natural history of HIV infection, and patterns of risk-related behavior. The model is fitted to the known history of the AIDS epidemic to date. It reduces our uncertainty about the dynamics of HIV infection and transmission by narrowing the range of possible values that certain important parameters take on. It also allows us to identify which uncertainties in the parameters contribute most to the uncertainties in our forecasts. Results indicate that the future incidence of CDC-defined AIDS is likely to be much higher than accepted U.S. Public Health Service estimates and that a self-sustaining epidemic among heterosexuals in the U.S. is already underway.

TP.60 HIV High-risk Indices among Anti-HIV-negative Blood Donors

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Transfusion Safety Study (TSS) is a multifaceted cooperative evaluation of factors influencing risk of transfusion-transmitted HIV infection and progression. As part of TSS, serum samples were stored from persons who were blood donors in September 1984 through January 1985, just prior to routine anti-HIV screening. Data are currently available about high-risk indices (known AIDS risk factors, hepatitis markers) for 114 anti-HIV(+) and 108 anti-HIV(-) control donors, matched to the former by sex, age, and area of residence. We have determined relative frequencies of high-risk indices in the two groups to assess possible discrepancies between presence of risk factors and anti-HIV status on screening.

Among anti-HIV(+) and anti-HIV(-) males, 41% and 1%, respectively, were homosexual; 42% and 0% were bisexual; and, 10% and 1% were IV drug users. Among anti-HIV(+) and anti-HIV(-) females, 50% and 0% had a known risk factor. The two anti-HIV(-)males with risk factors had a low intensity of exposure. For both sexes, anti-HBc positivity at follow-up 12 to 24 months later was 55% and 1%; ALT> 45 was 7% and 5%. In neither sex were there any instances of seroconversion at follow-up.

These data show a high proportion of bisexuals among donor males with homosexual contact; these men may be less likely than homosexual males to identify themselves as being in a risk group. The low frequency of high-risk indices among anti-HIV(-) donors with demographic characteristics similar to anti-HIV-(+) donors is reassuring about the sensitivity of present anti-HIV screening. (Supported by Contracts No. NO1-HB-4-7002 and NO1-HB-4-7003 of the National Heart, Lung, and Blood Institute.)

TP.61 Risk Factors for Infection by HIV and Development of AIDS in a Cohort of Gay Men.

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To identify factors predictive of either risk of infection by human immunodeficiency virus (HIV) or subsequent development of AIDS, we performed two case-control comparisons within a longitudinal study of 148 gay men. Eight HIV-seroconverters (SC) were compared to eight seronegative controls and 15 HIV-infected men who developed AIDS (DA) after entry were compared to 15 seropositive men matched for clinical status who did not progress. SC had fewer years of education (14 vs 16), whereas DA had more (16 vs 14). SC were more sexually active, especially in the year before seroconversion. DA were less sexually active throughout the period (1981-1984) antedating their diagnosis by 4-6 years. At entry, DA had lower white blood cell counts, hemoglobins, absolute number of CD4+ lymphocytes, total area of reaction to 3 intradermal antigens, serum albumin, and lymphocyte 5' nucleotidase than controls. IgG (ELISA) to a 20-amino acid synthetic peptide (p 62) from the alanine-glycine copolymer region of the Epstein-Barr Virus nuclear antigen (J. Immunol. 134:211, 1985) was lower than controls before and after both seroconversion and development of AIDS. We conclude that: 1) education and recent sexual behavior is associated with risk of infection, 2) sexual activity is diminished in infected gay men who develop AIDS compared to matched controls who do not, 3) multiple hematological and immunological variables differentiate those infected men at greatest risk of AIDS, and 4) low levels of IgG to an EBNA peptide may predict both increased susceptibility to HIV infection and development of AIDS.

TP.62 In Vivo Analysis of Antiretroviral Treatment Strategies in Mice.

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The reverse transcriptase inhibitor 3'-azido-3'-deoxythymidine (AZT) acts early in the retroviral life cycle, whereas α-interferon reversibly inhibits late events during retroviral propagation. AZT suppresses Rauscher murine leukemia virus complex (RLV)-induced disease in adult BALB/c mice. Longterm AZT treatment, however, leads to severe bone marrow depression. Recombinant human interferon α-A/D (rHuIFNα-A/D) strongly inhibits RLV-induced splenomegaly in BALB/c mice. Combining suboptimal doses of AZT and rHuIFNα-A/D leads to virtually complete suppression of splenomegaly without hematological toxicity. We conclude that AZT and rHuIFNα-A/D are highly synergistic in vivo.

We have also developed murine models to study retroviral neurovirulence, as well as in utero and perinatal infection, by infecting SWR/J mice as midgestation embryos or neonates with Cas-Br-E virus which causes hind limb paralysis. AZT given orally to pregnant and/or lactating females delayed the onset of paralysis and prolonged life of infected mice in a dose-dependent fashion. We conclude: 1) AZT is active in the CNS sanctuary, 2) AZT is effective across the placental barrier, 3) AZT is secreted into milk, and 4) pre- or perinatal infection and therapy can be evaluated in our model system. The significance of our studies lies in the rapid and cost-effective ways in which questions relevant to human neurovirulent retroviruses can be studied in vivo. Supported by a contract from the Commonwealth of Massachusetts Department of Public Health (RMR), a Faculty Development Award from the Pharmaceutical Manufacturers Association Foundation (RMR) and a Lucille P. Markey Charitable Trust Scholarship (AS). AZT was a gift from the Burroughs Wellcome Co., and rHuIFNα-A/D from Hoffmann La Roche, Inc.

TP.63 EVALUATION of a NEW VIRONOSTIKA HIV CONFIRMATION ASSAY
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In the Organon anti-HIV confirmation assay (CA) wells of Vironstika anti-HTLV III enzyme immunoassay strips (EIA) are preincubated overnight, respectively with blocking sheep anti-HIV serum, sheep anti-H9 serum and normal sheep serum. Thus HIV antibodies from a truly positive specimen can no longer bind to the HIV antigen. This blocking effect is compared with that of the anti-H9 serum. If the ratio of the optical density in the presence of the anti-H9 serum versus the reaction with the anti-HIV blocking serum is greater then 2.0, the sample isconsidered positive. A ratio between 1.5 and 2.0 is interpreted as doubtful or "gray zone" value. In this preliminary study 180 sera were tested in the EIA, CA and in two additional confirmation assays, indirect immunofluorescence assay (IFA) and immunoblot assay (IBA). The EIA results showed an overall concordance of 90.9 % with the CA. The CA revealed 4.3 % (4/94) false positive EIA results. These 4 negative CA results were confirmed by IFA and IBA. Concordance of the CA with IFA and IBA was 91.5 % and 94.5 % respectively. Two sera were negative in the CA, but positive in the IBA. One of them was also positive in the EIA and IFA and the other one was negative in EIA and IFA. Three sera (3.1 %) positive in EIA and CA could not be confirmed by IFA nor with IBA. All "gray zone" CA results were negative in IFA and IBA. An advantage of the CA is the use of the Vironostika anti-HTLV III EIA strips. This CA may be useful to confirm the positive result of a single performed EIA.

TP.64 Clinical and Behavioral Predictors of Developing AIDS and Related Outcomes among Asymptomatic HIV Seropositive Homosexual Men in Boston
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Seventy four of 290 asymptomatic (AS) gay men enrolled in a prospective study of the natural history of HIV infection between 1/85-5/86 were Ab(+) (25.5%). Of 57 followed for more than a year (≥ 1 visit every 6 months), only 12 have remained AS, whereas 35 developed persistent generalized lymphadenopathy (PGL), 9 thrush (2 with PGL), and 4 zoster. All 4 of the men who developed AIDS, had thrush first, whereas none of the men with zoster → AIDS; only 1 had prior PGL. Lifetime number of sexual partners, number of partners in the preceding 6 months, frequency of receptive anogenital exposure to semen, number of anogenital partners, drug use history and prior sexually transmitted disease history were not significantly different between men who remained AS and those with AIDS-related clinical outcomes. Whereas the polymorphonuclear cell count and hematocrit did not differ on the initial exam between those who stayed AS and those who got sicker, the mean number of lymphocytes was significantly different (p=.006) between the AS men (2250), those who developed PGL (1722) and those who → thrush, zoster or AIDS (1499). Thus, behavioral risk factors associated with becoming infected with HIV are not predictive of the development of PGL, thrush, zoster or AIDS; but thrush and lymphopenia are associated with early clinical progression towards worse outcomes.

TP.65 Prevalence and Incidence of AIDS, ARC and HIV Infection in a Gay NYC Cohort. JOHN L. MARTIN, Columbia U. School of Public Health,NYC,NY.

Prevalence and incidence rates of AIDS, ARC, and HIV infection (antibody) were calculated from data collected on a cohort of 745 NYC gay men. The AIDS-free sample was recruited and interviewed in mid-1985 in order to examine social and behavioral risk factors for AIDS and the presence of signs of ARC. An annual follow-up interview was completed one year later. Fourty-seven percent of the sample (N=357) underwent an initial serologic evaluation for HIV antibody in early 1986 and a follow-up blood sample was obtained six months later, at the time of the follow-up interview.

Prevalence of HIV antibody in early 1986 was 34%. Including the group of men with a history of sharing a needle for IV drug use increases this value to 36%. The six month incidence of seroconversion was two out of 230 seronegatives. Pro-rated for 12 months this represents an annual rate of 17.4 new infections per 1,000 susceptible gay men.

The prevalence of pre-AIDS conditions or symptoms of ARC [thrush,herpes zoster, lymphadenopathy, unexplained weight loss of 10 lbs (+), persistent unexplained fevers of 100°F (+), persistent unexplained diarrhea] during the 1984-85 year was 21% for the total sample and 38% for HIV antibody positive men. Incidence of new cases of ARC has not yet been calculated.

During the course of the one year follow-up interval, 18 incident cases of AIDS occurred. For the total sample this represents a rate of 24 new AIDS cases per 1,000 gay men. Using only HIV antibody positive men for the denominator, the annual incidence of AIDS is 67 per 1,000 HIV infected gay men.

The low seroconversion rate relative to the high AIDS incidence rate indicates that the rate of increase of new AIDS cases among gay men should decline in future years if sexual activity remains low or continues to decline at the rate we have previously reported.

TP.66 A Method for Estimating HIV Seroprevalence Rates in Urban Areas with High Rates of I.V. Drug Abuse: The Case of the Bronx
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In the absence of large scale seroprevalence surveys it is still possible, using available data, to estimate the probable magnitude and geographic localization of the AIDS epidemic in urban area with high rates of intravenous drug abuse (IVDA). The Bronx with 1.16 million people has a distinctive pattern of prevalence and distribution of AIDS, i.e., 69% of AIDS cases are among IVDA's, 20% are female, 89% are Black and Hispanic, and 4.5% are children. Local data on AIDS cases (by risk factors, age & sex) can be combined with local indices of the IVDA population, e.g., drug-related deaths and N.Y. State drug treatment data, to estimate numbers of IVDA's and rates of HIV seroprevalence. In this application of the model, HIV seroprevalence is calculated for Bronx males & females age 25-44, a group comprising 76% of all Bronx AIDS cases through November 1986; and for the South Bronx area where AIDS cases are most concentrated. Overall, the Bronx is estimated to have between 31,300 and 46,200 IVDA's of whom 78% fall into the 25-44 age group. 30%-50% of female IVDA's and 40%-60% of male IVDA's are considered to be HIV positive based on local sero-surveys. These figures produce a seroprevalence range of 5.3%-11.8% for all Bronx males age 25-44 and 1.1%-2.6% for females. For the South Bronx, with 66% of all IVDA's and 38% of the population, these rates are 9.3%-20.6% for males age 25-44, and 1.8%-4.3% for females. These must be considered minimum estimates of Bronx seroprevalence in this age group as they do not take into account the contribution of risk groups other than IVDA's. Implications for heterosexual and vertical transmission are discussed.

TP.67 Additional Evidence for Lack of Transmission of HIV Infection to Household Contacts of AIDS Patients.
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We report on the continuing enrollment and evaluation of non-sexual household contacts of adult AIDS patients (pts.). 200 contacts of 85 AIDS pts. were evaluated with detailed interviews, physical exams, and antibodies to HIV; 99 contacts were re-evaluated 6-12 months after cessation of household contact or death of the pt. Mean age of contacts 10.4 years; 57 under 6, 102 6-19, 41>19 years.

Median duration of household contact from 18 months prior to symptoms in pts. to last contact, 21 months. Median time elapsed from first contact during this period to last evaluation 35 months.

No household contact has AIDS. 199/200 are negative for serum antibody to HIV. One HIV+ biologic child of a woman with AIDS likely acquired infection perinatally.

Sharing of selected household facilities, items and personal interaction with AIDS patient among 199 household members:

Shared Activity	% Sharing	Days Shared (Median)	Days Shared (Cumulative)
toilet, bath, kitchen	85-89	586-616	102,793-106,357
comb	69	397	46,777
towels	48	418	36,937
utensils	38	108	16,402
plates	51	71	17,044
glasses	55	84	23,984
hugging	76	352	55,390
kissing	78	352	55,708

This study shows that household members remain at minimal to no risk for HIV transmission (95% CI,0-1.49) despite prolonged and substantial close non-sexual contact with AIDS patients, and after reevaluation 6-12 months after contact ceased.

TP.68 Western Blot-positive and -negative Sera from Harare, Zimbabwe and New York, NY, USA are identified Equally by a Synthetic Polypeptide-based Enzyme-linked Immunoassay (ELISA)
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Sera from 499 subjects seen at our institutions (434 from NY, 65 from Harare) were blindly assayed for reactivity with a new ELISA for HIV antibodies. The antigenic adsorbent for this system is a mixture of synthetic polypeptides representing highly antigenic epitopes of HIV gp41 and p25. Sera were selected on clinical grounds and/or known prior reactivity with currently employed ELISA techniques; 324 represented a wide spectrum of HIV infection (duration and clinical stage), 175 were controls. The control sera represented normal laboratory workers, parenterally and sexually exposed people, several primary immunodeficiencies, autoimmune diseases, thymoma, classical Kaposi's sarcoma, T and B non-Hodgkin's lymphomas and Hodgkin's disease. Most sera were assayed independently at both UBI and LIJMC and all ELISA results were compared with results from "Western" blots (WB). There were no false negatives, including 5 sera having no detectable band corresponding to gp41, one of which (AIDS-01) also lacked all reactivity on WB. There were also no false positive results. These data suggest that despite virus heterogeneity related to geographic distances, the epitopes in question remain invariate, and the assay is consistently highly sensitive.

TP.69 Prevalence and Persistence of HIV Antigen among IV Drug Users.

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Recently developed tests for detecting HIV antigen in serum provide a means for examining the role of serum antigen in the natural history of HIV infection. We examined the prevalence, persistence and sequelae of detectable HIV antigen in a cohort of 138 intravenous drug users in New York City. No subject had AIDS or ARC at the beginning of the study; each subject was seen twice with a mean of 9 months between the two data collection points. HIV antigen was assessed with the Abbott test, antibody was assessed with Abbott ELISA and Western blot tests.

Antigen was detected in 5/66 (8%) of the subjects who were initially antibody positive, in 0/4 of subjects who became antibody positive during the follow-up period, and in 1/68 (1.5%) of the subjects who were antibody negative at both the start and end of follow-up. All subjects who were antigen positive at the start of follow-up were also antigen positive at the end of the period; one antibody positive subject developed antigen during the period. Antibody to gp41 was more common than antibody to p24 in antigen positive subjects. Antigen was associated with increased rates of T4, T8 and B cell loss. 2/5 antigen positive, antibody positive subjects have since developed AIDS or died with ARC, compared to 3 of 61 antigen negative, antibody positive subjects ($p < .05$). (Disease incidence will be updated to the time of the conference).

Repeated ELISA antibody tests of the for one antigen positive subject were negative at both time points; repeated Western blots for this subject showed no antibody to p24, gp41 or gp120 at either time (additional testing is being conducted). This was the only subject for whom HIV antigen level declined.

Presence of HIV antigen in serum of IV drug users at risk for AIDS appears to be infrequent, relatively stable over time, and a potential marker for development of clinical disease. Further relationships among antigen presence, presence of specific HIV antibody, and other potential markers of disease progression will be presented.

TP.70 Factors Influencing the Risk of Infection with Human Immunodeficiency Virus in a Cohort of Homosexual Men - Denver 1983-1985

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We studied factors associated with infection with the human immunodeficiency virus (HIV) in a cohort of 231 gay men enrolled from November 1982 through May 1985, including 40 asymptomatic HIV antibody negative (AS-), 21 asymptomatic antibody positive (AS+), 74 with generalized lymphadenopathy (GLS), 39 with AIDS-related complex (ARC) and 57 with AIDS. Because univariate analysis did not show significant differences between AS+ and GLS or between ARC and AIDS, these groups were combined for analysis.

Riskfactors in past 4 months	AS- N=40 (%)	AS+/GLS N=95 (%)	ARC/AIDS N=96 (%)	Univariate analysis P*	P**	Multivariate analysis P***	Odds ratio (C.I.)
Enemas	3 (7.5)	49 (51.5)	32 (33.3)	<0.00001	<0.005	<0.0001	15.4 (4.1-58.3)
Receptive anal>30	1 (2.5)	24 (25.2)	12 (12.5)	<0.005	NS	<0.05	14.6 (1.7-126.0)
ARC/AIDS contact	3 (7.5)	24 (25.2)	13 (13.5)	<0.05	NS	<0.005	8.8 (2.2-35.3)
Sex partners>20	1 (2.5)	17 (17.8)	08 (08.3)	<0.05	NS	0.062	8.1 (0.8-75.1)
IV drug use	2 (5.0)	19 (20.0)	21 (21.8)	<0.05	<0.05	0.063	5.0 (0.9-27.5)
Insertive anal>50	2 (5.0)	43 (45.2)	21 (21.8)	<0.05	NS		

*AS- vs AS+/GLS; **AS- vs ARC/AIDS; ***AS- vs AS+/GLS C.I.=Confidence interval

In multivariate analysis (table) the use of enemas, number of episodes of receptive anal intercourse and sexual contact with someone with AIDS or AIDS related conditions were all independently associated with HIV infection. IV drug use and number of sexual partners improved the multivariate model but did not reach statistical significance. In univariate analysis the ARC/AIDS group did not differ significantly from AS- as to number of episodes of receptive or insertive anal intercourse and number of sexual partners, but this most likely represents confounding that occurs when current risk factor behavior in fatally ill men is used in place of risk factor behavior at the time of HIV transmission. It indicates however that this group has become less sexually active and that HIV infection is largely spread by relatively healthy infected men.

TP.71 Mortality in AIDS in Colorado: Life-Table Analysis from the AIDS Reporting System.

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Although there have been over 30,000 cases of AIDS reported in the USA, there have been surprisingly few comprehensive analyses of mortality in AIDS patients (pts). In 1985 DCS implemented the computerized AIDS Reporting System (ARS), which utilizes PRODAS software program provided by the Centers for Disease Control (CDC). From May, 1982 through December 31, 1986, 309 adult cases of CDC-defined AIDS were reported, of whom 202 (65%) had died. Follow-up morbidity and mortality information was ascertained on 304 (98%). Those whose survival was not ascertained were censored as of the last diagnostic entry in the ARS.

Median survival (MS) from time of diagnosis of all pts was 239 days (d), of pts who initially presented with Pneumocystis pneumonia (PC, n=182) 257 d, Kaposi's sarcoma (KS, n=65) 293 d, PC and KS (n=10) 223 d, other opportunistic diseases (OD, n=52) 140 d, and PC who survived at least 60 d after diagnosis (n=115) 337 d. MS by transmission category was for gay men (n=221) 250 d, gay men and IVDU (n=48) 236 d, heterosexual and IVDU (n=13) 251 d, hemophiliacs (n=7) 68 d, heterosexual contacts (n=5) 293 d, transfusion recipients (n=5) 320 d, and no identified risk (NIR, n=10) 87 d. MS for pts with lymphoma at any time (n=26) was 137 d compared with no lymphoma (n=283) 260 d; and for disseminated cytomegalovirus (CMV, n=50) 198 d and no CMV (n=259) 255 d. MS for pts with or without mucocutaneous herpes, M. avium-intracellulare, Candida esophagitis, cryptosporidiosis, and cryptococcosis was not significantly different.

Pts who present with OD have a worse prognosis than KS and/or PC, and PC pts who survive their initial episode have the best prognosis. NIR pts have a significantly worse prognosis than other transmission categories, probably because diagnoses are delayed. Lymphoma and CMV indicate a worse prognosis, although CMV may be underdiagnosed. ARS is useful for following prognosis in different types of AIDS pts, and for monitoring trends over time.

TP.72 REVERSIBILITY AND PROGRESSION OF PERSISTING AIDS-RELATED COMPLEX

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A cohort of 693 HIV antibody positive homosexual men in Los Angeles were characterized as being asymptomatic (well), having persistent generalized lymphadenopathy (PGL) or AIDS Related Complex (ARC) on two separate visits at least 6 months apart and were re-examined 6-12 months later. ARC was defined as one or more of the following reported conditions: fever or diarrhea lasting more than two weeks or involuntary weight loss greater than 9 pounds. Men were considered to have PGL if examination revealed non-contiguous lymph nodes greater than 1 cm in diameter at 2 or more non-inguinal sites. Men who had been in that same status at the subsequent consecutive visits were most likely to remain in that same status at the subsequent visit. The AIDS attach rate was highest for those with a diagnosis of ARC on two consecutive visits (12%) but was lower and similar (4-7%) among the other groups PGL/PGL, well/well, ARC/PGL, PGL/ARC. The ARC attack rates were similar and lower for those with any sequential status other than ARC/ARC. These observations suggest that persisting ARC is an unfavorable prognostic sign, although at least some men with persisting ARC do revert to either PGL or well, at least temporarily. PGL alone does not appear to be an unfavorable prognostic sign over the time span studied. For the meeting, we will have data from an additional 1000 seropositive men in Baltimore, Chicago and Pittsburgh.

TP.73 Predictors of The Hazard of AIDS Among HIV Seropositive Gay Men.

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Of 4,955 gay men who enrolled in a prospective study, 1828 were seropositive for HIV at entry. Among the seropositives, 164 (9.0%) developed AIDS during 24 months of follow-up. Exposure variables of interest, with data collected at entry and at three subsequent six-monthly visits, included age, race, adiposity, sexual activity, CBC, T-cell subsets, serum immunoglobulins, serum antibody to CMV and HIV, serum HbsAg, and AIDS-related complex (ARC). Follow-up data were available on 1820, 1614, 1454 and 1332 participants at the four respective visits. We conducted a stratified analysis using a proportional hazards regression model. In an attempt to control for the unknown time since infection, the strata were defined by the entry CD4 number (a known marker of disease progression) and the rate of change in the number of CD4 cells. The estimates of the relative hazards from the multivariate analysis for those variables that made independent significant contributions to the final model were:

	AIDS	KS	OI
Age	1.51 for 10 yrs.	1.79	1.50
log CD8	2.10 for twice	1.89	2.18
$\log_2$ IgA	1.37 for twice	1.54	1.38
Hemoglobin	1.20 for -1 gm%	1.19 (NS)	1.26
HIV antibody	1.79 for -1 O.D.	1.19 (NS)	2.02

When Kaposi's sarcoma (KS) and opportunistic infection (OI) were analyzed separately, the hazard of KS was more strongly associated with older age, while the hazard of OI was more strongly associated with increased number of CD8 cells and decreased level of HIV antibody. In summary, after adjusting for number at entry and change in CD4 cell number, several other variables have predictive information regarding the development of AIDS.

TP.74 Clinical Significance of Anti-HIV Antibodies in Asymptomatic Blood Donors: A Prospective Study.

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88 asymptomatic Western blot + (WB+) blood donors and 51 EIA+, WB- control donors have thus far been enrolled in a 5-year prospective study. Compared with the WB- controls, WB+ individuals were more frequently male (88% vs 59%) and black (51% vs 6%). The probable source of HIV exposure was homosexual contact, 75%; heterosexual contact, 17%; IV drugs, 1%; unknown, 7%. None were transfusion related. On initial evaluation of WB+ subjects: 1) 38% had extra-inguinal lymphadenopathy; 2) mean T_4 cell number was 450 (range 120 to 982) and mean T_4/T_8 ratio was 0.75 (range 0.26 to 1.7); 3) 47% had diminished in vitro responses to tetanus and 25% had decreased responses to PHA and/or PWM; 4) 45% had IgG > 1800 mg/dL; and 5) 2% had platelets < 100,000/ul. HIV was isolated from only 8 of 88 (9%) cultured at Biotech and 7 of 74 (10%) cultured at CDC. This is markedly lower than earlier CDC studies (57% viral isolation) and suggests a change in the constituency of the WB+ donor population, as also implied by questions relating to lifestyle.

On initial visit, 55 (62%) were CDC group II and 33 (38%) CDC group III. During 6-18 months of follow-up, one donor progressed to group IV A and one to group IV C-1 (pneumocystis). In these patients, the interval from enrollment to disease was 16 and 12 months, respectively. T_4 cell number and in vitro immune responses showed progressive deterioration in these two individuals, and virus was isolated just prior to onset of clinical disease.

None of the EIA+, WB- control donors were in known HIV risk groups and none had evidence of HIV-related disease, immune impairment, or positive viral cultures. We believe these represent false positive reactions and support reinstatement of such donors into the donor pool.

TP.75 Heterosexual Transmission of AIDS in New York City

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Although heterosexual transmission of HIV is reported to be the most common mode of transmission in Central Africa and Haiti, the extent to which this virus will spread among heterosexuals in the USA is unknown. We examined New York City Dept. of Health (NYCDOH) and national surveillance data to evaluate the patterns of heterosexual risk behavior among AIDS cases. The 8681 cases reported in NYC through 1986 account for 30% of the total US cases. Approximately 2% of both NYC and total US cases occur among heterosexual partners of risk group members (NYCDOH classifies persons from Haiti/Central Africa separately). Through 1986, 182 sex partner cases were reported in NYC; 3 males and 179 females. All female partners of the male cases were IVDUs. Risks of the male partners of the female cases were as follows: 153 (85%) IVDUs; 20 (11%) bisexual; 3 (2%) Haitian or Central African; 2 (1%) bisexual IVDUs; 1 (1%) hemophiliac. In NYC sex partner cases have remained at about 2% of the total cases since 1982. Infected heterosexual IVDUs comprise the major reservoir of HIV for the heterosexual population. While the 2570 cases among heterosexual IVDUs in NYC account for 53% of US IVDU cases, NYC sex partner cases account for only 36% of the sex partner cases: male cases are 3.5% and female cases 42% of the 509 US sex partner cases. Differences between NYC and US data may be due to better risk identification through more thorough case investigation by NYCDOH. NYC surveillance data suggest that heterosexual transmission does occur and females appear to be at greater risk than males. To avoid further heterosexual transmission in NYC, effective prevention strategies should include a broadly based education program, but focus on the major source of HIV in the heterosexual community, infected IVDUs.

TP.76 Survival Analysis of Children Reported with AIDS in New York City, 1982-1986.

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The incidence of Acquired Immunodeficiency Syndrome (AIDS) in children under age 13 continues to increase in New York City (NYC), but the course of illness and prognosis remains incompletely described. One-hundred forty seven children have been reported with maternally transmitted AIDS from 1982 through 1986. Median age at onset of symptoms of immunodeficiency was five months and at diagnosis of first opportunistic infection was 11 months. Survival analysis was performed on the 114 with either Pneumocystis carinii pneumonia (PCP) or Lymphocytic Interstitial Pneumonitis (LIP). For 87 children with PCP, median survival from birth was 14 months (Interquartile (IQ) range=29 mo.). Median survival was longer for 42 females than for 45 males (19 vs 11 mo.). Hispanic males had the poorest median survival, at six months for 15 with PCP (IQ range=19 mo.). Median survival for 26 children with LIP who never had PCP is strikingly different at 91 months. Numbers of cases in different racial and diagnostic groups are too small to be compared statistically. Seven children, aged four to nine years have survived three or more years beyond initial diagnosis. PCP as primary diagnosis was present in one, LIP in five, and both diagnoses in one. These data confirm the very different course of HIV-infected children who present with LIP vs. PCP. Differences in therapy must be examined in future survival analyses.

TP.77 Fatal Unconfirmed Cases of AIDS in Dallas, Texas.

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The current AIDS surveillance definition underestimates the magnitude of mortality associated with AIDS and the widespread availability of HIVab testing after June, 1985 has added a new dimension that permits an examination of HIV associated mortality. Reports were obtained from physicians, infection control practitioners, and other sources including review of all death certificates. Suspects were investigated by a nurse epidemiologist. From 1981-86, 474 Dallas residents were reported as having AIDS, of whom 281 (59.3%) had died by December 31, 1986. An additional 371 persons were reported by physicians and other sources as possible cases of whom 42 (11.9%) died before December 31, 1986. Two died of suicide (1 was known HIV positive). Another 34 were known to be HIV positive: 15 did not meet the criteria for the AIDS surveillance definition (4 were transplant recipients, 3 had received steroid therapy for non-malignant conditions, 4 had disseminated infections [1 TB, 3 coccidiodomycosis], and 4 had lymphomas or leukemias). Another 19 died of illnesses suggestive of AIDS, but confirmatory diagnostic tests were lacking: 6 persons underwent diagnostic procedures, not resulting in diagnosis, and 13 had no diagnostic procedure: none had a post-mortem. The proportion of deaths possibly attributable to HIV are underestimated by 6% to 10% due to lack of diagnostic procedures and post-mortem examinations. In the future physicians may be less aggressive in AIDS diagnosis, resulting in greater underestimations of HIV mortality.

TP.78 HIV Sero-Survey of Post-Partum Women at a Municipal Hosptial in New York City.

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We performed a sero-survey of all new mothers admitted to the obstetrical service of a municipal hospital serving the urban poor. Cord blood was used for HIV testing; all women, on the day after delivery were interviewed for HIV related risk factors. Blood samples and questionnaires were given a code number and personal identifiers were destroyed prior to testing.

Six hundred women delivered: complete data is available on 527. The remaining delivered on weekends or were discharged before interview. One hundred twenty-three of 527 women(23%) had a self reported risk factor; 404 (77%) had no known risk factors. All samples were tested by ELISA and confirmed by Western Blot (WB). Women with risk factors had a WB done even if the ELISA was negative. Thirteen samples, 2.45% (1.4-4.3,% 95% C.I.), were Western Blot postive (WB+); 11 of which were also ELISA positive. Eight positive samples were in persons with risk factors (3 IVDA, 1 Haitian, 1 multiple sex partners 1 transfusion, 2 with a sex partner who used drugs). Thus 8/123(6.5%) of women with a risk factor were positive. Five of 404 (1.2%) samples from non-risk group women were positive.

Taking an appropriate medical history concerning risk factors for the purpose of HIV counselling and testing during early pregnancy will only identify 61% of the infected population at our institution. Testing of the entire prenatal population at our hospital would be required for identification of the remaining 39% of seropositive women.

TP.79 MALNUTRITION AND HIV ANTIBODY PREVALENCE IN THE CENTRAL AFRICAN REPUBLIC.

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HIV antibody prevalence has been studied simultaneously in mothers and their malnourished children, in a rural area of the Central African Republic (CAR). Children were selected on the basis of their nutritional status i.e. moderate protein energy malnutrition (P E M), kwashiorkor or marasmus. The results obtained from rural area have been compared to those previously obtained in an urban pediatric population as well as those recorded in the general population of the CAR.

Elisa was used for sera screening, while Western Bloc allowed us to confirm the presence of anti HIV 1 antibodies when reacting with either GP110, GP41 or both.

Anti HIV 1 as well as HIV 2 antibodies are absent in the healthy control group of children of less than 15 years, while they are found in 12.3% of the malnourished children of the urban area as compared to 3.9% in the rural area.

These differences do not seem to be due only to environmental factors but more likely to the way of life of the mothers of sick children under investigation.

TP.80 Western-blot in HIV seroconversion : the importance of detecting anti gp 110/120, the earliest envelope antibodies.

L. NOEL and the RETROVIRUS GROUP OF THE FRENCH SOCIETY OF BLOOD TRANSFUSION - Paris, France

We present a Western-blot (w-b) study of anti-HIV antibodies in sequential sera collected from 25 individuals at the time of seroconversion and beyond. W-bs were carried out with commercially available kits from BIOTECH-DUPONT, BIORAD and DIAGNOSTIC PASTEUR. The strips loads in gp 110/120 and gp 41 antigens were systematically controlled. In 6 cases seroconversion was proved by the discovery of a positive whole virus anti-HIV ELISA less than one month after a previous negative test. In 19 cases the incomplete pattern observed in w-b on the first positive sample was suggestive of early seroconversion and indeed simultaneous study with samples collected later demonstrated the completion to a typical positive anti-HIV w-b pattern. On the first positive samples the antibodies observed were only : anti-p 25 (with the strongest signal), faint anti-p18 and p55 and anti- p110/120. Anti p 41 were never detected at this early stage but appeared on samples collected 3 weeks to as long as 3 months later.

Considering existing cross-reaction with *gag* gene products in w-b, the criterion of anti HIV specificity relies on the detection of antibodies directed against an *env* gene product. We emphasize the importance of using w-b filters rich in gp 110/120 in confirmatory tests to allow for an earlier diagnosis and a better discrimination between true positives and non HIV specific reactions.

TP.81 Neutralizing Antibodies against HIV in Relation to AIDS related Diseases.

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Seventy consecutive frozen serum samples collected over a 1-5½ year period from 10 HIV (Human Immunodeficiency Virus) antibody positive individuals were tested in a microplate ID_{50}assay for neutralizing antibodies (NA) against a Danish HIV isolate and the results related to disease outcome. Virusproduction was monitored by a microplate reverse transcriptase assay. Total anti HIV was titrated in ELISA and antibodies against core and envelope proteins detected by Abbott's HTLV-III confirmatory assay.

One patient reached stable titers of NA > 1:640 ½ year after seroconversion, and 3 patients around 1:100 after 2 years. One patient had titers < 1:100, and 5 patients permanently titers between 1:10 and 1:20. The 4 patients with titers > 1:100 remained healthy during the entire observation period (2½-4½ years). One of the 6 patients with titers < 1:100 developed AIDS, one Hodgkins Lymphoma (HL), one ARC, and 3 remained healthy.

The titer of total anti HIV varied between 1:740 and 1:90000 and correlated to the titer of NA. The titerratio (ID_{50}/ELISA titer) varied appr. a 100 fold indicating the neutralizing capacity is probably a function of quality as well as quantity of the antibodies. In all serum samples antibodies against envelope proteins were detected. Two patients lacked antibodies against core proteins (CPA) (1 AIDS, 1 HL, ID_{50}<1:20). Two patients lost CPA (1 ARC, ID_{50}< 1:100, 1 healthy ID_{50}= 1:100). The remaining 6 healthy patients had CPA during the entire observation period.

In conclusion, NA may thus be a prognostic factor since patients with titers > 1:100 in this study remained healthy during the entire observation period.

TP.82 CLUSTER OF HETEROSEXUAL TRANSMISSION OF HIV IN BRUSSELS.

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A 48y. old single central African engineer was found to have ARC in 1985. He died in July 1986 with HIV encephalitis and pneumonia. He lived in Belgium since 1965, travelled regularly to Central Africa and had no history of homosexuality, IV drug use, or blood transfusion. Contact tracing allowed identification of 19 women (12 middle-class Europeans, 7 Africans; mean age: 35y.) who had had sexual contacts (only vaginal) with the index case in Brussels during the last 7 years. 8/19 women were married and mean number of children was 1.7 (range 0-4). Number and duration of sexual contacts with the index case ranged from one to multiple contacts during two years or more. 17/19 women have been examined and 10 of them (59%) (7 Europeans, 3 Africans) had antibodies against HIV (demonstrated by ELISA and Western blot). The index case was the only potential source of infection for the white women for whom no sexual promiscuity (less than 3 partners/y.), no travel to Africa, no sexual contact with other men belonging to high risk groups for HIV, no IV drug use and no transfusion was found. 7/10 seropositive women described mononucleosis-like symptoms of acute HIV infection between 1983 and 1985. The current clinical status of the seropositive women is presently: generalized lymphadenopathy (n=6), AIDS-Related complex (n=2), AIDS (n=1) and unknown in one case. The male sexual partners of these women (all Belgian) are currently under investigation.

This cluster demonstrates how HIV could spread heterosexually in an European area with low prevalence of HIV infection from a few number of promiscuous men to a high number of female sexual partners without classical risk factor for HIV infection.

TP.83 TRANSMISSION OF HTLV III (HIV) IN INFANTS OF SEROPOSITIVE MOTHERS.

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HIVinfection in pediatric age occurs most frequently in children of infected mothers by transplacental or perinatal transmission. To assess the risk for the fetus to acquire HIV infection during pregnancy we selected and followed up 36 infants born to HIV antibody positive drug addicts by vaginal delivery. None of them was breast fed or received blood or blood products. All the mothers were in WR1 or WR2 disease stages. All the infants seen at birth had HIV antibodies at high levels, comparable to that of their mothers. 56% of those presently older than 6 months had progressively decreasing HIV antibodies and lost them between 7 and 12 months of age, suggesting only transplacental maternal antibody crossing without infection. This is further confirmed by the lack of clinical symptomatology and failure to detect HIV antigen in serum and in peripheral blood lymphocyte culture, as opposed to seropositive symptomatic children. The risk for the offspring of WR1 or WR2 staged mothers of acquiring HIV infection during pregnancy can be presently estimated to be around 44%. Failure of detecting HIV antigen in serum and in cell culture may be useful as a diagnostic tool to rule out infection.

TP.84 Lack of Evidence for New Transmission Modes Among AIDS Patients.

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As of January 23, 1987, 29,582 AIDS patients (29,159 adults, 423 children) had been reported to CDC. Of these, 97% fit into risk groups that suggest a possible means of disease acquisition. For 3%, means of acquisition is undetermined. Of all AIDS patients initially identified with undetermined risks and available for follow-up, 72% were reclassified because risk factors were identified (68%) or the patient was found not to meet the surveillance case definition (4%). Of the 932 AIDS patients with currently undetermined risks, information is incomplete on 215 because of death (158), refusal to be interviewed (39), or lost to follow-up (18). Of the remaining 717 patients, 523 are currently under investigation. No risk was identified for 194 patients who were interviewed or for whom other follow-up information was obtained. However, 39% of the patients (52/134) answering a standardized questionnaire gave histories of other sexually transmitted infections. Some of the patients with undetermined risks may not have HIV infection: for those on whom HIV-antibody information is available, 9% (32/349) tested negative compared with 1% (103/7330) for AIDS patients with identified risks. Lack of evidence for new transmission modes is clearest in the 5- to 15-year age group, which makes up 16% of the U.S. population. Sixty-six AIDS cases (0.2% of total cases) have occurred in this age group, which is exposed like other groups to casual contact with HIV-infected persons, insects, and environmental factors. Of these, 65 (98%) fit into established risk groups; the remaining case is lost to follow-up. The proportion of patients with undetermined risks has not increased significantly over time (p>0.10).

TP.85 Serological Analysis of HIV gag Reactive Sera in a Blood Donor Population Using Both Viral and Recombinant Antigens

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Sera from a normal blood donor population that display reactivity in an HIV-ELISA screening kit (DuPont) have been further analyzed using both viral and recombinant antigens. Two major patterns of HIV immunoreactivity have been identified in these HIV-ELISA reactives. The predominant class were gag reactive env non-reactive, and largely consisted of sera reacting with p15/p17 bands on immunoblot. These sera comprise 50% or more of HIV-ELISA reactives examined. Specificity of antibodies to HIV gag was confirmed in several ways, including competition between viral and recombinant antigen for reaction with blood donor antibodies. Competition experiments also provided a direct demonstration that HIV-ELISA reactivity in these blood donors is largely caused by antibodies that react or cross-react with HIV gag. An HIV env reactive class of sera was also identified in this population based on screening with both HIV immunoblots and with a recombinant (ENV9) ELISA. The gag immunoreactivity may indicate exposure of this population to an as yet unidentified retrovirus.

TP.86 Prevalence of HIV antibodies in healthy subjects and groups of patients in some parts of Tanzania

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Sera from groups of healthy subjects and from groups of patients collected in 1986 in Dar es Salaam (the capital of Tanzania), Bukoba (the capital of the Kagera region in the north west corner of Tanzania) and Arusha (in the north east part of Tanzania) were screened for antibodies to Human Immunodeficiency Virus (HIV) by ELISA (Organon-Teknika). All screening positive sera were also tested by a HIV competitive ELISA (Wellcome) and by Western blot analysis using disrupted virions of the HTLV-III B strain of HIV as antigen. In Dar es Salaam Western blot confirmed HIV antibodies were demonstrated in 3.6% of 192 pregnant women, 28.8% of 225 barmaids, 4.4% of 225 male blood donors, 9.25% of 400 male patients attending a clinic for sexually transmitted diseases, in 86% of 35 patients with herpes zoster and in 94% of 83 patients with clinically suspect AIDS. In Bukoba the prevalence of HIV seropositivity was higher, namely 16% among 100 pregnant women and 14% among 36 blood donors while in Arusha only one out of 144 (0.7%) pregnant women and none of 42 barworkers tested were positive. HIV infection seems to be newly introduced in Tanzania and the extent of spreading of the infection differs in various parts of the country.

TP.87 Mortality, AIDS Incidence and Immunologic Abnormalities Among Intravenous Drug Abusers (IVDA) in New York City (NYC): A 5-Year Prospective Study. STANLEY H. WEISS*, I.B. MARGOLIS**, R. ZELNICK**, H.M. GINZBURG*, D. FUCHS***, J.J. GOEDERT*, et al., *National Institutes of Health, Bethesda MD, **Queens Hosp. Center, Jamaica NY,***Univ. of Innsbruch, Austria.

IVDA in NYC were among the first recognized AIDS cases. In 1981 in NYC we initiated the earliest prospective study of IVDA to evaluate clinical and immunologic abnormalities. HIV antibodies (Ab) were present in 46% of 54 IVDA by 1982. At least 24% of those HIV seronegative in 1982 had seroconverted by 1986. Overall, at least 60% of the original 60 IVDA now have HIV Ab.

Seven seropositive IVDA have died, a total mortality of 42% ±15% at five years (Kaplan-Meier method, median follow-up 46 mo., range 0-63 mo.). Deaths were due to AIDS (3), car accident (1), and causes still under investigation (3). By five years, AIDS has been documented in 17% ±10%.

Mortality among the seronegative IVDA also has been substantial: 9% ±6% (median follow-up 54 mo., range 0-64 mo.), with deaths due to drug overdose and stabbing. None of the seroconverters has developed AIDS (median observation after seroconversion 12 mo., range 2-24 mo.).

Mean T4a counts and T4a:T8 ratios were significantly lower in prevalent seropositive IVDA compared to seronegatives (792 & 0.95 vs. 1175 & 1.40, $p<0.02$). Immunologic pertubation was intermediate in seroconverters. Immune activation as measured by neopterin was increased among T4a deficient IVDA.

The high mortality among IVDA from all causes makes careful prospective follow-up of both seropositives and seronegatives essential. A review of post-mortem material from one subject who had died of an apparent overdose revealed AIDS (Military Med 151:M33). The excess mortality among seropositive IVDA may indicate under-ascertainment of HIV-related disease in IVDA.

TP.88 Relative Risks of AIDS for American Blacks and Hispanics RICHARD M. SELIK, M.F. Rogers, AIDS Program, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia, USA

Although non-Hispanic blacks and Hispanics represent only 12% and 6%, respectively, of the U.S. population, they constitute 25% and 14%, respectively, of the 29,497 AIDS patients of known race/ethnicity reported to the Centers for Disease Control (CDC) from June 1, 1981, to January 26, 1987. We studied their greater risk of AIDS, compared with that for non-Hispanic whites, in terms of their relative risks (RR), assessed as the ratio of the cumulative incidence of AIDS in a particular racial/ethnic group to the cumulative incidence in whites. The cumulative incidence was calculated as the total number of AIDS cases per million population of the same racial/ethnic group. Based on AIDS cases reported to CDC and population data from the 1980 census, the cumulative incidence of AIDS in whites was 98; that in blacks, 283; Hispanics, 290; and other groups (e.g., orientals), 63; these figures yielded RR of 2.9, 3.0, and 0.3 for blacks, Hispanics, and other groups, respectively, as compared with 1.0 for whites. The RR for blacks and Hispanics were greater for women (14.0 and 10.9) and children (14.0 and 9.1) than for men (2.9 and 3.1). When the analyses were stratified by the probable means of AIDS acquisition, the RR were greatest for transmission categories associated with intravenous drug abuse: for heterosexual intravenous drug abusers (IVDA) (21.3 and 23.5), for other persons whose heterosexual sex parters were IVDA (24.2 and 31.3), for children whose mothers were IVDA (36.4 and 25.5), and for children whose mothers had sex partners who were IVDA (14.5 and 23.1). The RR were also increased in association with male bisexuality, blood transfusion, and absence of any identified means of acquiring AIDS. Knowledge of these associations may be important in targetting AIDS prevention strategies for blacks and Hispanics.

TP.89 Five-Year (1982-1987) Prospective Clinical and Immune Evaluation of Hemophiliacs Before and After Exposure to HIV. CHRIS TSOUKAS*, H. STRAWCZYNSKI†, F. GERVAIS*, J. SHUSTER*, P. GOLD*, *Montreal General Hospital, †Montreal Children's Hospital, Montreal, Canada.

Immediately following the first appearance of AIDS among hemophiliacs in 1982 we evaluated 34 adults with severe classic hemophilia for immune deficiency, all were treated exclusively with lyophilized Factor VIII concentrates. Initially all felt well and none had clinical manifestations related to AIDS although 68% had evidence of cellular immune dysfunction. To determine the significance of this dysfunction and to assess the long term clinical outcome of this cohort, the group was followed for the next 5 years. They were examined and tested semiannually for T cell subsets, serum immunoglobulins, lymphocyte responsiveness to mitogens, anergy, and viral serology. Serum samples were sequentially frozen and stored.

Subsequent HIV serology by Western blot analysis revealed that initially 60% were seropositive in 1982 and by 1984 33/34 had seroconverted. Although all were initially healthy and asymptomatic, today 90% have clinical manifestations of HIV disease. 52% (17/33) have persistent generalized lymphadenopathy (CDC Group III classification) and 38% (13/33) have AIDS or AIDS-related syndromes (or Group IV). One patient has died of AIDS related disease, two are critically ill following Pneumocystis carinii pneumonia and 5/33 have developed severe life threatening thrombocytopenia. All HIV seropositive individuals currently display a spectrum of progressively deteriorating in vitro immune parameters that correlate significantly with time of exposure to HIV.

We conclude that the majority of HIV seropositive severe classic hemophiliacs will develop severe HIV disease five years following exposure to the human immunodeficiency virus and almost all will display a progressive and significant deterioration of their immune status.

TP.90 EPIDEMIOLOGY OF HIV INFECTION IN HONG KONG PCK LI EK YEOH WK CHANG YY CHAN SH LEE KL THONG
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In a seroepidemiological study of the prevalence of HIV infection in Hong Kong, individuals from different groups were tested for HIV antibodies using a commercially available ELISA method. Positive results were confirmed by immunofluorescence and Western Blot.

74 of 38,293 individuals screened between April 1985 to December 1986 were confirmed to be seropositive. Analysis of the results at 6-monthly intervals showed no increase in the prevalence of seropositivity.

RESULTS OF HIV SEROLOGY

	No. Tested	No. (%) HIV +ve
Social Hygiene (STD) Clinic	35088	7(0.02%)
IV Drug Abusers	1127	0(0 %)
Haemophiliacs	102	46(45.1%)
Patients with Cooley's anaemia	306	0(0 %)
Haemodialysis patients	379	1(0.26%)
Health Care Personnel	219	0(0 %)
Sermen donors	85	0(0 %)
Government Hospitals&Clinics	745	8(1.1 %)
Private Hospitals & Clinics	242	12(4.9 %)
	38293	74(0.19%)

RISK FACTORS IN 63 INDIVIDUALS SEROPOSITIVE FOR HIV

	No AIDS	AIDS	Total
Haemophiliacs	46	0	46
Homosexual/ Bisexual	10	2	12
Heterosexuals with prostitute contact	2*	1	3
Transfusion recipients	2+	0	2
	60	3	63

*1 practised IV drug abuse in Spain
+Both received blood in 1984

Haemophiliacs with a history of imported factor VIII transfusion, homosexuals and bisexuals, and heterosexuals with history of sexual contact with prostitutes constitute high risk groups for HIV infection in Hong Kong. The risk of transfusion-related HIV infection should be reduced by the donor screening programme instituted since August 1985.

TP.91 Modelling the Incidence of Acquired Immunodeficiency Syndrome (AIDS) in New York, San Francisco and Los Angeles JOHN PICKERING, J.A. WILEY, L.E. LIEB, J. WALKER, and G. RUTHERFORD, Dept. of Entomology, Univ. of Georgia, Athens, GA; Survey Research Center and San Francisco Men's Health Study, Univ. of California, Berkeley, CA; County of Los Angeles, Dept. of Health Services, CA; City of New York, Dept. of Health, NY, and City and County of San Francisco, Dept. of Public Health, CA.

With an epidemic model we explore the biology and sociology of AIDS incidence and forecast new cases. Our model assumes that AIDS can be modelled as a sexually transmitted disease. Its parameters reflect (1) how long AIDS takes to develop after exposure to the infectious agent, (2) when infected individuals are contagious, (3) decreases in transmission rates because of behavioral changes, and (4) saturation--the removal of susceptible individuals through infection. Declines in anal/rectal gonorrhea cases in New York and San Francisco are used in modelling the impact of behavioral changes.

By November, 1986, New York, San Francisco, and Los Angeles had over 8,031, 2,546, and 2,360 AIDS cases, respectively. Each city's cumulative number of cases doubled in the 10-13 months before July, 1985, but may not continue to increase at this rate. The model shows how AIDS incidence in the cities could level off and even start to drop by 1991, because of saturation and behavior. However, a sensitivity analysis of the model's parameters shows that there are insufficient data to choose between radically different forecasts. Before accurate forecasts can be made, more data are needed on (1) the distribution of development times, (2) the infectivity of individuals, (3) the proportion of infections that develop AIDS, and (4) behavioral changes.

Judged by the model's fit to the cases reported by November, 1986, it appears that these cases generally were diagnosed 3-4 years after exposure to the agent and were most infectious in the months immediately after exposure.

TP.92 Evaluation of first and second generation (confirmatory) assays for antibodies to HIV P. Nico LELIE, J.G. HUISMAN et al.(1)
Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, (CLB), incorporating Lab. of Exp. and Clin. Immunology University of Amsterdam.

The sensitivity and specificity of six commercial enzyme immunoassays (EIAs) for antibodies to HIV has been evaluated in 6488 serum samples (Lancet, August 30, 1986: p.483-486) (1). This panel and sequential sera from 12 individuals who seroconverted for anti-HIV were used to compare the first and second generation EIAs from three manufacturers (Abbott, Organon, Wellcome) and three confirmatory assays, i.e. Western Blot (WB, Biotech Dupont); competitive immunoassay for separate detection of antibodies to HIV envelope and core (CIA, Abbott) and a home-made radio immunoprecipitation assay (RIPA-CLB). The confirmatory tests and second generation EIAs were significantly more sensitive in detecting antibodies early after HIV infection than the first generation EIAs. The earliest detectable antibodies in the confirmatory tests were anti-p24 and anti-gp120/160 in WB; anti-envelope in CIA and anti-p24 in RIPA. The anti-core CIA did not detect anti-p24 responses in approximately 10% of asymptomatic seropositive individuals. The antibody levels against envelope proteins gp 160/120/41 persisted during transition to AIDS, whereas antibody titers to p24 diminiminished or disappeared. Follow up studies showed that false positive reactions were observed in confirmatory tests. The respective frequencies in a panel of tricky sera (n=293) and of blood donors (n=5000) were W.B.: anti-p24 1,7% , 0.18% ;CIA anti-envelope: 0,3% , 0.02% ; RIPA anti-p24: 0% , 0.06%.The new generation EIA's are important tools to establish early antibody responses in patients and blooddonors exposed to HIV.

TP.93 PRELIMINARY RESULTS OF A SURVEILLANCE SYSTEM OF HIV PEDIATRIC INFECTION

GIUSEPPE IPPOLITO, PEDIATRIC AIDS AND HIV INFECTIONS WORKING GROUP,
Coordinated by Latium Region Epidemiologic Unit and Children's Hospital Bambino Gesu- Rome- Italy

A surveillance system of HIV infection, based on compulsory notification by laboratory physicians of every positive subject together the relevant data (place and date of birth, sex, place of residence, risk factors) was set up in Latium, a 5.000.000 inhabitants region of Italy, in 1985.
An active working group to trace seropositive mothers, contact and perform clinical follow up on babies at risk was established.
80 babies (1 hemophiliacs, 2 transfused and 77 child born HIV positive mother) had a positivity for anti-HIV antibodies until October 1986.
73 seropositives have been enrolled in a follow-up study.
Mean time of observation was 10.3 months (range 1-36), for a total of 749 person/month of observation.
Nine cases of AIDS have been observed. Incidence rate, in a period of 36 months, is .123 (CI 95% .058-.221).
Fourteen children (.122 - CI95% .109-.301) have lost the anti-HIV antibodies during the first year of life (mean 8 months, range 5-12).
Thirty-five children (.479 CI 95% .361-.600) younger than 1 year (mean time of observation: 4.1 months) were positive at the end of the observation time.
Six subjects (.082 CI95% .031-.17) were seropositive and asymptomatic at the end of an average observation period of 17.8 months.
Five (.068) children showed a persistent generalized lymphadenopathy after a mean 12.4 months of observation and four babies (.055) costitutional diseases and/or secondary infectious diseases.

TP.94 Surveillance of AIDS in India With Special Reference to Union Territory of Delhi.

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Following the first confirmed evidence of AIDS virus infection in India in April, 1986, a massive surveillance campaign was launched to screen high risk individuals across the country. From July through December,1986, a total of 5,000 serum samples were collected from specified high risk individuals from Union Territory of Delhi. Of them 3268 were from males and the rest (1732) females, mostly between 20-45 years of age. The samples belonged to patients attending STD clinics (2789), prostitutes (408), jail inmates (413), drug addicts (49), professional blood donors (1057), chronically ill patients referred from hospitals from HTLV-III antibody screening (246), foreign students (8) and the patients who underwent by-pass surgery abroad (30). All the samples were subjected to Wellcozyne HTLV-III EIA. Only one sample yielded a strong positive result in ELISA confirmed by Western blot. Samples from two male patients attending STD clinics yielded positive ELISA results but only one gave a mild positive ($_{p24}$ band only) result in Western Blot.
These findings indicate that AIDS virus infection in this part of the country is probably at a very low key, but continued surveillance is warranted to keep a close vigil over the situation.

TP.95 ACTUAL SITUATION OF HIV INFECTIONS IN FRENCH POLYNESIA

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Since July 1985, a serological survey is carried out in 682 subjects belonging to different groups at risk for AIDS. Positive sera in ELISA were confirmed by immunoblotting. The sero prevalence in January 1987 is :

0/33 hemodialysis patients transfused in Tahiti

0/131 female prostitutes

1/138 male homosexual (transvestites). He never left French Polynesia and reported foreign sexual partners.

10/244 (9/170 M, 1/74 F) homosexual or bisexual men and patients attending private practitioners or STD clinic for AIDS counseling. 9 of them have lived or travelled often in countries where AIDS is endemic.

6/125 (4/54 M, 2/71 F) permanent residents operated mostly between 1981 and 1985 for heart disease and intensively transfused in other countries (France essentially) before blood screening is established.

1/11 (5 M, 6 F) household contacts or sexual partners of 3 seropositive cases.

The overall prevalence rate of HIV antibodies is 2.5 % in the high risk population and 0.1 ‰ as referred to the total population (170 000 inhabitants). ARC has been diagnosed in 4 of them. Introduction of the AIDS virus is likely recent since no instance has been found yet in more than 8 000 blood units tested in the local transfusion center. As a matter of fact, HIV has been brought into French Polynesia in part, by a much-travelled class of the population involving homosexual and bisexual men essentially and in the other hand by heterosexual patients who underwent heavy surgery in foreign country.

TP.96 Genetic Aspects of AIDS in Trinidad.

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Trinidad has a population of 1.2 million comprising people of African descent 41%, Indian descent 41%, mixed race 16%, Chinese 1% and Caucasians 1%. To date a total of 144 cases of AIDS have been seen in Trinidad. Of these 133 have been in people of African and mixed African descent, 7 in people of Indian descent, 3 in Caucasians and 1 Chinese. The common opportunistic infections seen are candidiasis, toxoplasmosis, histoplasmosis and cryptococcosis. Less commonly seen is Pneumocystis carinii pneumonia and Kaposi's sarcoma is rare.

In a survey of 106 healthy homosexual men in Trinidad in 1983, 36/90 (40%) of those of African and mixed African descent were HIV seropositive compared with 6/16 (37.5%) of those of Indian descent. As the prevalence of homosexuality appears to be equal in the various ethnic groups in Trinidad the possibility of a genetic factor associated with the relative paucity of cases of AIDS in Indo-Trinidadians was considered. Preliminary studies of antibody dependent cell-mediated cytotoxity (ADCC) have shown that HIV positive Indo-Trinidadians without disease have higher levels of ADCC (mean 29.4%) than Afro-Trinidadians without disease (mean 14.8%). Initial studies of HLA haplotypes among 130 healthy males in Trinidad have shown that HLA Dr 5, which is present in 24.8% of black Africans is absent thus far in 70 Afro-Trinidadians while present in 8.5% of Indians. In addition, there is a relative absence of HLA Dr w6 (4.3% vs 20.2%) and particularly HLA Dr 1 (0% vs 15%) in persons of Indian descent in Trinidad compared with those of African ancestry.

These genetic differences could possibly expain the discrepancy in the occurence of AIDS among Trinidadians of African and Indian descent.

TP.97 AUTOLOGOUS KILLING MECHANISMS IN HIV INFECTION.

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Longitudinal studies performed among hemophiliacs (H) infected by the human immunodeficiency virus (HIV) reveal a progressive loss of CD4 lymphocytes and increased numbers of CD16 and activated CD8 cytotoxic lymphocytes. We asked if lymphocytes of HIV infected H could kill autologous cells. In 4 h. chromium release assays, unstimulated H lymphocytes (n=9) demonstrated significant cytotoxicity against autologous cells (5.2±2.0% lysis) (mean ± SE), whereas controls' (C) cells (n=12) demonstrated no autologous killing (0.5±0.3% lysis, $p<0.02$). After culture for seven days with irradiated autologous peripheral blood mononuclear cells (n=7) nonadherent (NA) H cells demonstrated enhanced killing of autologous PHA blasts when compared to C (n=7) (11.5±4.8 vs 4.1±2.0% lysis $p<0.05$). After stimulation by alloantigens, H NA cells demonstrated greater killing of autologous targets than C NA cells did (19.4±4.2 vs 10.0±2.5% lysis, $p<0.01$) and were activated more than C NA cells to lyse both allogeneic (stimulator) targets ($p<0.03$) and unrelated allogeneic targets ($p<0.05$). Cold target inhibition studies demonstrated that K562 tumor cells and unrelated PHA blasts inhibited lysis of autologous targets. Yet cell separation studies revealed that autologous killing was mediated by CD8 lymphocytes and was unaffected by depletion of CD16 cells. Enhanced autologous killing was seen in 3 HIV-infected homosexual men but not in 3 HIV-seronegative H. Thus, lymphocytes of HIV-infected persons possess low levels of cytotoxic activity against autologous lymphocytes and show increased activation by alloantigens to lyse nonspecifically autologous and allogeneic cells. Autologous killing may contribute to the progressive lymphopenia of HIV infection.

TP.98 **Persistent Co-Infection of T Lymphocytes with HTLV-II and HIV and the Role of Syncytium Formation in HIV-Induced Cytopathic Effect.**

DAVID C. MONTEFIORI*, W. EDWARD ROBINSON and WILLIAM M. MITCHELL, Vanderbilt University, School of Medicine, Nashville, Tennessee.

We previously demonstrated a high permissiveness of HTLV-II-transformed T lymphocytes (C3) to human immunodeficiency virus (HIV) infection in vitro, and that this infection results in the lysis of cells (D.C. Montefiori and W.M. Mitchell, Virology, 155, 726-731, 1986). We now show that a small percentage of HIV infected C3 cells resist cell lysis, grow continuously in culture and express antigens of both viruses. High levels of reverse transcriptase activity found in the culture fluid of these co-infected cells was associated with the presence of fully infectious HIV and an absence of detectable infectious HTLV-II. Virus production in C3 cells co-infected with HIV isolate HTLV-III was approximately 3-fold greater than in C3 cells co-infected with the HIV isolate LAV, a result which suggests that HIV genomic diversity may give rise to differences in replicative capacities. Lysis resistance was found to be a cellular-determined function in that HIV produced in cultures of C3/HTLV-III cells retained the capacity to elicit a lytic response upon repeated infection. Small syncytia were rarely observed in cultures of C3 and non-lytic C3/HIV cells whereas large syncytia were in abundance during the lytic phase of co-infection, a result which supports a role for syncytium formation in the mechanism of HIV-induced cytopathic effects. The results of these studies also demonstrate that there exists a lack of HIV interference by HTLV-II infection, and that HTLV-II transformed lymphocytes could act as a chronic reservoir for HIV in vivo. These findings have important medical implications in view of the high prevalence of HTLV-II antibodies in HIV antibody positive and negative individuals at risk for AIDS (Robert-Guroff et al., JAMA 255, 3133-3137, 1986).

TP.99 Effects of long term seropositivity to Human Immunodeficiency Virus in a cohort of homosexual men.

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The long term effects of HIV infection were evaluated in a cohort of homosexual men by comparing clinical and lab parameters obtained from 2 visits a mean of 18 months apart in groups of 148 persistently seropositive and 287 persistently seronegative men. Differences between the groups were present at each visit with the seropositive men exhibiting lower CD4 counts, higher CD8 counts, lower CD4/CD8 ratios, higher C1q binding, higher IgG and IgA levels, lower Hgb, and lower lymphocyte counts. More important, comparison of the differences between visits in the positive and negative groups, revealed that the seropositive group underwent a significant mean decline in the CD4/CD8 ratio (-0.13 vs +0.05; p=.013), and significant mean rises in the C1q binding (+4.7 vs +0.5; p<.001), in the IgG (+92 vs -2; p<.001) and in the IgA (+16 vs +1; p<.001) as compared to the seronegative group. Seropositive men were at elevated risk of developing symptoms and lymphadenopathy, though these risks did not progress with time. Comparisons of parameters obtained a mean of 21.4 months prior to diagnosis in 11 seropositive men who subsequently progressed to AIDS and 134 seropositive men who did not, revealed lower CD4 counts (450 vs. 739; p<.001),lower CD4/CD8 ratios (0.65 vs 1.14; p<.001), higher C1q binding (20.7% vs. 13.6%; p<.001), lower Hgb (14.6 vs 15.1; p=.088), and lower lymphocyte counts (1638 vs. 2041; p=.041) in those who progressed to AIDS. Moreover, between antecedent visits, those who progressed to AIDS experienced greater mean declines in CD4 count (-155 vs -40; p=.074), in Hgb (-1.1 vs -0.1; p<.001) and in WBC (-1000 vs -351; p=.079) than the seropositive AIDS-free group. Although these data document long term effects of HIV infection in a seropositive cohort, about 25% of persistently seropositive men maintained normal CD4/CD8 ratios, suggesting the possibility of one subgroup of men who may be resistant to the effects of HIV infection, and another who are particularly susceptible to the progressive effects of HIV that precede the development of AIDS.

TP.100 Antibodies to the transactivating protein of HIV, tat3 and the induction of HIV antigen expression in vivo.

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To obtain large amounts of the tat3 protein, a plasmid was constructed in which the 3th to last tat3 codons were fused to the first 52 codons of the E.coli galactokinase gene in the pOTSKF33 expression vector. The fusion protein was induced in E.coli using nalidixic acid and purified using preparative SDS-PAGE. The purified fusion protein had a molecular weight of 17 KD and was used as antigen for immunoblotting and enzyme-linked immunosorbent assays (EIA). The presence of HIV Ag was evaluated by EIA (Abbott Labs, N. Chicago, Ill.). Sequential sera of 86 individuals, collected over a period of two years were used in this study Twenty-one of these individuals seroconverted for antibodies to HIV and 65 were HIV-Ab seropositive at entry in the study. Among the HIV-Ab seropositives 21 were HIV-Antigen positive throughout the study and 27 seroconverted for HIV-Ag. The presence of antibodies to tat3 was closely related to expression of HIV-Ag in serum ($p<0.01$). Seroconversion for antibodies to tat3 was observed prior to or concomitant with seroconversion for HIV-Ag. Individuals with a prolonged HIV antigenemia showed a steady decline in antibody titers to tat3 with time. These results present evidence for in vivo regulation of HIV gene expression by the tat3 protein.

TP.101 Characterisation of the T-lumphocyte Response to Primary HIV Infection.

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Multiple T-lymphocyte determinations were availabe on 19 homosexual men for up to 500 days following primary HIV infection.

In all subjects the initial response to HIV infection was a marked decrease in the total lymphocyte count and in the absolute numbers of circulating T4+ and T8+ cells; the T4+:T8+ ratio remained normal. Within 14 days the lymphocyte count began to rise with a T8+ subset increasing proportionally more than the T4+ subset, leading to an inverted T4+:T8+ ratio by day 20. This period was followed by an increase in the total lymphocyte count (and subsets) above base line levels. This relative lymphocytosis lasted up to two months and the major contributing subset was the T8+ lymphocytes, followed by an incomplete reduction in T8+ lymphocytosis. The ensuing months were characterised by a return of the T4+ lymphocytes to near-baseline levels, but a maintenance of a high T8+ response and an inverted ratio.

These changes represent three distinct phases: an acute symptomatic period with lymphopenia, a recovery period with a T8+ lymphocytosis, and a longer term period of asymptomatic HIV infection with a normal level of T4+ lymphocytes, slightly increased T8+ lymphocytes and an inverted T4+:T8+ ratio.

Further investigations of the mechanisms of these changes and the role of T8+ lymphocytes in limiting HIV infection may improve understanding of immunoregulation of HIV infection.

TP.102 Rapid Detection of Human Immunodeficiency Virus Antigens in Lymphocytes by Immunogold Scaning Electron Microscopy.

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The observation by scanning transmissión electron microscopy (STEM) of -- gold immunolabelled Human Immunodeficiency Virus (HIV) infected cells might be a new approach to rapid diagnosis of AIDS at the early phase of infection. It combines both the morphological information and rapid procedures of scanning electron microscopy (SEM) with SEM of lymphocytes from 13 HIV positive individuals and from HIV infected cultures lymphocytes reveals the presence of giant cells with characteristic "spongy" surface appearance that - suggest viral infection. In 4 patients, other unnusual spherical multifaceted structures (5-18 um.) have been also found. They could correspond with a process of gene amplification and could indicate virus production at low level.

A more precise detection of the presence of HIV antigens in these "spongy" cells has been achieved by their specific indirect inmunolabelling, using - anti-p17 and anti-gp41 monoclonal antibodies as aprimary antibodies and 30 nm gold-labelled goat anti-mouse IgG as secondary antibodies. The use of - STEM techniques and backscattered electrons imaging for gold detection provides a very sensitive technique for antigen detection at and below the -- cell surface. Paired electron micrographs have been taken showing that -- "spongy" cells have a particulate gold content, indicating HIV infection.

TP.103 Normal Neutrophil Phagocytosis but Impaired Chemotaxis in Homosexual Male Patients with AIDS, ARC and Neither Disorder

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Although the target cell for HIV infection is acknowledged to be the T4 helper cell, monocyte, macrophage and B-cell function is also adversely affected by the retrovirus. We and others have previously reported an increased incidence of unusual and recalcitrant bacterial infections in patients with AIDS as well as homosexual males suggesting impairment in neutrophil function. Chemotaxis and phagocytosis are critical events in the effector functions of granulocytes. Thirty-one homosexual or bisexual males were studied for neutrophil chemotaxis using zymosan-activated serum in a Boyden chamber and phagocytosis utilizing latex spheres. Twenty-three patients had AIDS, 5 had ARC and 3 had neither. Seventeen of 23 (74%) with AIDS, 4 of 5 (80%) with ARC and 2 of 3 (67%) with neither disorder expressed defective chemotaxis but normal neutrophil phagocytosis. No distinguishing clinical or laboratory characteristics could be discerned within each group that separated normals from those with abnormal leukocyte chemotaxis. It is concluded that defective chemotaxis is common in patients with AIDS, ARC, and in otherwise healthy HIV antibody-negative homosexual males. The etiology of this defect will require additional studies, but appears to be related to lifestyle rather than to HIV infection.

TP.104 In vitro synthesis of antibodies against HIV-1 components.

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We studied the in vitro synthesis of antibodies directed against human immunodeficiency virus, type 1 (HIV-1, LAV/HTLV-III) components (HIV-Ab) from peripheral blood lymphocytes of 30 seropositive individuals. A significant amount of HIV-Ab was detected by an IgG-ELISA assay on culture supernatants of unstimulated cultures. Mean absorbance values in the patient group was 1.104±0.381 SD, whereas in the control group mean values of 0.020±0.02 SD were found. The phenomenon reflected a de novo Ig synthesis, as shown by the inability of puromycin-treated cultures to produce HIV-Ab. Moreover, spontaneous HIV production was detected within the first 24 hr of culture, suggesting an in vivo activation of antibody-forming cells. When PBL were cultured in the presence of pokeweed mitogen, a significant difference in HIV-Ab production between seronegative and seropositive individuals was still observed. When examined by the Western blot technique the supernatants from seronegative subjects gave negative patterns, whereas all those from seropositive individuals were reactive with different virus proteins. A general correlation between serum and supernatant Western blot reactivity was observed, although in individual cases some antibody specificities were not detected in culture supernatants. The present in vitro model could be an useful tool to investigate the immunobiology of HIV-1 infection.

TP.105 CD4-gene transcription is not impaired by HIV replication.

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HIV infected cell lines display decreased CD4 membrane expression and mRNA levels after long-term cultures. Two mechanisms could explain such bulk reduction in CD4-gene transcription: (1) direct genomic interaction between HIV and CD4; (2) progressive selection of individual CD4 low-producing cells.Using the cytodot technique with a β-actin internal standard, we sequentially performed semi-quantitative determination of CD4 mRNA levels in normal lymphocytes and various cell lines before and after infection with HIV. Normal or slightly elevated CD4 mRNA was observed during early (<2 weeks) HIV replication in normal CD4+ lymphocytes. CD4 mRNA remained also normal at the chronic replication phase (>2 weeks) in CEM derived clones. In both cell types, HIV replication led to the complete disappearance of detectable surface CD4.Low CD4- expressing HIV-resistant cells eventually emerged from the lines while the clones subsequently died from cytopathic effect. Altogether all these findings rule out any direct genomic interaction between HIV and CD4,arguing for the selection of low CD4-expressing cells in heterogeneous cell lines. They confirm and emphasize previous results that strong CD4 expression is a requisite for the occurrence of significant HIV cytopathic effect.

TP.106 Regulation of HIV Expression in Acutely Infected Promonocyte Cells and in Chronically Infected Promonocyte Clones

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The monocyte has emerged as a potentially important cell in the pathogenesis of human immunodeficiency virus (HIV) infection. Successful HIV infection of normal monocytes in vitro has been achieved. In addition, The promonocyte cell line, U937, has been demonstrated to be susceptible to infection with HIV, and the level of HIV expression has been shown to be under regulatory control with cytokines such as GM-CSF and INF-γ.

The present study has investigated the effect of phorbol myristate acetate (PMA) an inducer of monocyte differentiation, on the initial infection of U937 cells with HIV and on chronically infected U937 clones. Following acute infection of U937 cells with HIV the cell line can be inhibited from producing virus if treated with 10^{-10} M PMA. Concomitant with this inhibition, PMA induces differentiation of U937 cells as manifested by adherence, granule formation, increase in surface density of CR3, and down-modulation of CD4 (the HIV receptor). In contrast to the acutely infected U937 cells, clones derived from the chronically infected U937 population which manifest only a very low level of viral productivity show an increase in the level of HIV expression after PMA induction. EM studies of these clones indicated that PMA also induced increased endocytotic vesicles containing many HIV particles. In situ immunofluorescence of these clones stained with pooled sera from AIDS patients showed an increase from 2% to 30% positivity after PMA treatment. These studies lend insight into the role of monocyte differentiation in the susceptibility to HIV infection as well as provide a model at the clonal level to delineate latency or chronicity of HIV infection of monocytes and the signals required for conversion to high level viral expression.

TP.107 THE SKIN REPRESENTS A SITE OF VIRUS REPLICATION DURING INFECTION WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV).

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The skin is a heterogenous organ consisting of cells of different ontogenetic origin. Epidermal Langerhans cells(LC) represent a persistent, distinct population of antigen presenting leucocytes within the skin. We have recently demonstrated that LC of HIV-infected individuals react with monoclonal antibodies directed against HIV specific core proteins p17 and p24 - a finding highly indicative for the presence of HIV within these cells.

Extensive electronmicroscopic analysis of skin and mucosal biopsies from an AIDS patient with anti p17/p24 reactive LC now revealed mature HIV-like virions in the extracellular space surrounding LC as well as developmental forms of HIV- like particles budding from LC surface membranes. Moreover, cocultivation of a punch biopsie from normal appearing skin of this AIDS patient with mononuclear phagocytes from a non-infected donor, resulted in the detection of high levels of reverse-transcriptase activity in the culture supernatant. This latter finding implies that active virus can be rescued from the skin of HIV infected individuals.Our findings conclusivly confirm that (I) LC are an actual target for HIV infection and production, supporting the view that besides T cells , cells of the monocyte /macrophage lineage are a major target population of this virus (II) the skin may serve as a viral reservoir during the course of HIV infection.

TP.108 HIV Binding to the CD4 Molecule: Conformation Dependence and Antibody Inhibition.

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The human immunodeficiency virus (HIV) binds to $CD4^+$ T cells via a complex of the viral envelope glycoprotein gp110 and the CD4 molecule. We treated virus with a variety of physical, chemical, and enzymic agents to determine their effect on the capacity of HIV to bind to $CD4^+$ T cells. Reduction and alkylation (but not alkylation alone) and trypsin digestion (but not glycolytic enzyme digestions) of HIV destroyed its capacity to bind. Human sera reactive with HIV universally inhibited virus binding, but the binding inhibition titers were only weakly correlated with anti-gp110 titers. Absorption, elution, and crossabsorption of anti-HIV serum with immobilized native or reduced and alkylated virus provided evidence for conformation-dependent antibodies that are potent inhibitors of virus binding. Taken together, these results indicate that the CD4 binding site of gp110 requires a proper tertiary protein conformation that is dependent on covalent disulfide bonds and that conformation-dependent antibodies are elicited that are potent inhibitors of virus binding.

TP.109 Frequency of Infected CD4 Cells After in vitro Exposure to HIV Determined by Limiting Dilution Analysis.

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We developed a limiting dilution assay for determining the frequency of infected cells (FDIC) after in vitro exposure to HIV. Cells were incubated with HIV, washed, diluted, and cocultured with phytohemagglutinin (PHA)-stimulated lymphocytes in microcultures. The frequency of positive cultures conformed to a Poisson distribution. The assay was sufficiently sensitive to detect a single infected cell as assessed by analysis of HIV-infected H9 cells. The FOIC depended on the ratio of virus to cells used for inoculation, i.e. the multiplicity of infection (MDI). For example, the FOIC for PHA-stimulated CD4 cells increased from 1 in 24 at a MDI of 0.99 to 1 in 1 at a MDI of 99. FOIC increased with increasing time of incubation with virus and reached a maximum of 1 in 5 to 1 in 1 at 24 hours for PHA-stimulated CD4 cells. Inoculation of unstimulated CD4 cells under the same conditions yielded FDIC that were substantially lower (less than 1 in 100). Activated cells were treated at various times after exposure to HIV with trypsin under conditions sufficient to inactivate accessible HIV and to remove the HIV-binding portion of the CD4 molecule. There was no difference in FOIC with or without trypsin, suggesting that the physical manipulations used remove surface-bound virus. In contrast to these results, HIV binding to the CD4 receptor is trypsin-sensitive, occurs much more rapidly, and is equivalent in activated and nonactivated CD4 cells, indicating that the limiting dilution results reflect a more rate-limiting step in the establishment of cellular infection, such as penetration of virus. We conclude that virtually all CD4 cells, under optimal conditions of activation and incubation, can be infected with virus. However, establishing infection is more efficient in activated cells, possibly related to increased internalization and cycling of the CD4 molecule.

TP.110 Production of Antibody by Circulating B Cells of HIV-Seropositive Subjects.

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Cells producing antibody (Ab) do not normally circulate except during a short time following immune stimulation. In patients infected with HIV, however, circulating B cells were found to spontaneously secrete anti-HIV antibodies in 20 of 22 cases. For these experiments, 0.1-5.0 x 10^5 peripheral blood mononuclear cells (PBMC) were cultured in microtiter wells without mitogen or antigen for periods of 1-15 days. At 5 x 10^5 cells/well, cells from five control subjects produced no detectable anti-HIV Ab (measured with commercial ELISA kits) over the entire culture period; at this cell concentration, cultures from 5 of 6 AIDS patients spontaneously produced Ab. Cells from 11 of 11 patients with ARC produced Ab and cells from 4 of 6 HIV-seropositive subjects without AIDS or ARC (high risk patients) also produced Ab. Positive cultures showed the presence of detectable Ab within 24 hr., indicating that these cells had been stimulated in vivo. Incorporation of HIV viral lysates into the medium (0.125-1.0 μg/ml) for varying periods of time did not enhance Ab production. By a radio-immunoprecipitation assay, Ab production appeared polyclonal, with reactivity primarily directed against gp 41, gp 120 and reverse transcriptase. When PBMC were cultured at lower concentrations, wells containing Ab-producing cells were detected in all experiments at 2.5 x 10^5 cells/well and in 75-80% of experiments at 1.0 and 0.5 x 10^5 cells/well. No Ab production was detected at <0.5 x 10^5 cells/well. The presence of circulating Ab-producing cells may reflect continual antigenic stimulation by replicating virus in infected subjects.

TP.111 A genetic factor affecting susceptibility to HIV infection and to disease progression.

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Whilst examining serum factors in AIDS patients, many were noted to have a rare phenotype of Group specific component (Gc). This prompted an indepth study of Gc phenotypes in 214 subjects from existing cohorts of homosexuals at risk from, or infected by HIV, classified according to current clinical status, compared with 122 healthy male heterosexual seronegative controls. Sera were analysed by isoelectric focusing on thin layer polyacrylamide gels containing ampholytes (pH 4.5- 5.4).

30.2% of AIDS patients were homozygous for Gc 1 fast (cf controls 0.8%; $p<0.001$); other seropositive clinical groups also more commonly had Gc 1f. Seronegative asymptomatic homosexual contacts of AIDS patients (AH-p) lacked this phenotype. By contrast, AIDS patients lacked the Gc 2 phenotype, but this was more common in the AH-p group (25%) than in controls (9%; $p<0.01$). A chi squared trend test showed a highly significant association between the Gc 1 fast allele and progression to AIDS ($p<0.0001$) and the reverse with Gc 2 ($p<0.05$). We propose that Gc is involved in viral entry into host cells and that the different allelic forms of Gc, which vary in sialic acid content, dictate its ease.

TP.112 Serum Non Organ Specific Autoantibodies during Infection of Human Immunodeficiency Virus (HIV).

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HIV infection is associated with polyclonal B cell activation and hypergammaglobulinemia. Autoimmune features may be present. Data are lacking about the occurrence of serum non organ specific autoantibodies. 64 HIV infected subjects, including healthy carriers (HC) and patients with LAS, ARC and AIDS, were screened for antibodies to: smooth muscle (SMA), nuclei (ANA), intermediate filaments (IMF), microfilaments (MF) (IFL on rat kidney and HEp-2 cells, 1:40 serum dilution) and extractable nuclear antigens (ENA) (CIE, undiluted serum).

	HC(15)	LAS(28)	ARC(13)	AIDS(8)	tot.(64)
SMA	3(20%)	7(25%)	7(54%)	5(63%)	22(34%)
ANA	4(27%)	9(32%)	4(31%)	1(13%)	18(28%)
anti IMF	3(20%)	6(21%)	5(38%)	3(38%)	17(27%)
anti MF and anti ENA	0	0	0	0	0

SMA positivity showed always the V pattern and was associated with anti IMF ($p<0.01$). The number of circulating CD4 lymphocytes was higher in SMA+ than SMA- AIDS patients ($p<0.05$). The autoantibodies status did not correlate with: circulating platelets and immune complexes, serum gammaglobulins, cutaneous anergy.

Serum non organ specific autoantibodies do occur in HIV infected patients with the same pattern (SMAV with anti IMF reactivity) of other viral infections. It is not known whether HIV itself can trigger the process. The SMA prevalence increases with the disease progression.

TP.113 EVALUATION OF D/Dr^+ $B1^+$,$CD4^+$ $4B4^+$, $CD4^+$ $2HB4^+$LYMPHOCYTE SUBSETS DURING THE EVOLUTION OF HIV INFECTION.

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The prognostic meaning of D/Dr^+B1^+,$CD4^+4B4^+$,$CD4^+2HB4^+$ lymphocyte subsets during the evolution of HIV infection was investigated in the following subjects: 13 HIV-Ab positive only, 48 LAS, 28 ARC and 9 AIDS with Pneumocystis carinii pneumonia. Monoclonal antibodies were supplied by Coulter Immunology and Becton Dickinson and were used with the Coulter lysing procedure. Dual-color flow cytometric analyses were performed with EPICS V.

In the patients (pts) HIV-Ab positive it was demonstrated a decrease only of the $CD4^+4B4^+$ subset (388±150/ml vs n.v. 564±233/ml: $p<0.01$). The reduction was more remarkable in the further stages: LAS 343±197/ml ($p<0.01$), ARC 278±218/ml ($p<0.01$) AIDS 34±25 ($p<0.01$). The $CD4^+2H4^+$ lymphocytes were decreased in ARC, 170±145/ml vs n.v. 279±165/ml ($p<0.01$) and AIDS 31±20/ml ($p<0.01$).The $CD4^+4B4^+/CD4^+2H4^+$ ratio showed a progressive diminution from simple HIV-Ab positive pts 1.93±1.18/ ($p<0.01$) to full blown AIDS, 1.2±0.49 ($p<0.01$). The $D/Dr^+/B1^+$ lymphocyte subset displaied a significative decrease from the LAS to the AIDS group.

Our data suggest thet the early loss of the $CD4^+4B4^+$subset of lymphocytes is the most consistent change in lymphocyte subpopulation and shows to be progressive from siple HIV-Ab positivity to AIDS. This aspect is consistent with the T-independent stimulation of B lymphcytes commonly reported and appears to be a premonitory sign of immunological deterioration.

TP.114 Production, Characterization and Epitope Mapping of a Human Monoclonal Antibody Reactive with the Envelope Glycoprotein of HIV

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To analyze the humoral response to HIV infection, we sought to generate monoclonal antibodies from HIV seropositive individuals. B lymphocytes from an HIV antibody positive patient were transformed with Epstein-Barr virus, then fused to a mouse-human heteromyeloma fusion partner. Immunoglobulin containing supernatants were screened for anti-HIV reactivity by indirect immunofluorescence analysis. Reactivity was confirmed by Western blot and radioimmunoprecipitation analysis (RIPA). Using this approach, we have identified a monoclonal IgG antibody, 1B8.env, reactive with the envelope glycoprotein of HIV. The antibody specifically stains acetone fixed HIV-infected cells and is also reactive with viral antigens expressed on the surface of unfixed infected cells. In Western blot and RIPA the antibody is reactive with the precursor (gp160) and transmembrane (gp41) forms of the HIV envelope glycoprotein. Using a lambda gt11 expression library, we have definitively mapped the epitope recognized by 1B8.env to a 47 amino acid region of gp41. This epitope appears to be largely conserved among multiple distinct HIV isolates, based on conservation of this region in published sequences of distinct HIV isolates and on preliminary experiments with 1B8.env and a panel of viral isolates. Additional studies of biological activity (neutralizing capacity and cytotoxicity) are in progress. These results demonstrate the feasibility of our approach for generating human monoclonal antibodies to HIV for analysis of the humoral response to HIV and for other applications.

TP.115 HTLV-I and HIV Co-seroprevalence in AIDS Non-Hodgkin's Lymphoma Patients: Characterization of AIDS Lymphoma Cell Line, AL-1

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HTLV-1 and HIV seroprevalence was examined by Western blot and immunoprecipitation analyses in 3 patient groups to determine the relationship of these retroviruses to the development of B cell non-Hodgkin's lymphoma (NHL). All NHL patients(18/18), 5% of AIDS patients (1/20) and 14% of healthy HIV seropositive gay men (14/100) had antibodies to HTLV-1 envelope determinants.

To test whether HIV or HTLV-I might be directly involved in AIDS lymphomagenesis, we established a tumor cell line (AL-1) from a co-seropositive gay man with Burkitt's lymphoma. Southern blot analysis of cell line AL-1 DNA revealed the presence of EBV genomes, but not HIV or HTLV-I. Monoclonal antibodies to the envelope glycoprotein of HTLV-I (gp61/68) identified rare (1-2%) infected mononuclear and macrophage-like cells within lymphoma tissue sections of AL-1. Tumor tissues were negative for HIV p25 antigens. AL-1 produced an antibody, IgMk, that recognized the HTLV-1 envelope gp61. Defining further the epitope specificity, we used the lambda gt11 expression vector cloning scheme to identify a 40 amino acid segment within gp61 that was recognized by the AIDS AL-1 IgM. These data suggest that HTLV-1 or a similar retrovirus may play a role in the genesis of AIDS associated NHL through a process of chronic antigenic stimulation.

TP.116 Loss of Suppressor Cell Function in HIV+ Individuals

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Elevated T cell responses to HLA alloantigens (ALLO) have been reported in ~50% of AIDS patients and HIV^+ asymptomatic individuals (J. Immunol. 137: 2514, 1986), as well as in ~50% of HIV^- homosexual men (J. Immunol. 135: 3163, 1985). In contrast, terminal AIDS patients appear to have lost ALLO T cell reactivity. This T cell response to ALLO is not dependent on $CD4^+$ helper cells (Ibid, 1986). To determine the mechanism responsible for this elevated ALLO T cell immunity, we have identified a suppressor cell (or circuit) which is functional in most HIV^- heterosexual men. This type of suppression is dependent on a radioresistant macrophage that is adherent to plastic. The suppresion: a) appears to be HLA self restricted; b) when preactivated in vitro, affects T cell responses to viruses as well as to ALLO; c) is most efficiently activated in vitro by ALLO stimulation; and d) can be abrogated in vitro by infection with influenza virus. This suppressor system is not detected in HIV^+ individuals nor in AIDS patients who exhibit elevated ALLO T cell activity. Since a) a CD4 independent pathway (detected by ALLO) provides some immune function in AIDS patients; b) this pathway is elevated by removal of suppressor cell activity; and c) AIDS patients appear to have lost the suppressor function; modulation of the immune system by this regulatory mechanism and its abrogation in high risk and HIV^+ individuals may play a role in HIV susceptibility, progression to AIDS in HIV^+ individuals, and/or maintenance of some immune protection during the earlier stages of symptomatic AIDS.

TP.117 ABSOLUTE DEFICIENCY OF INTERLEUKIN 2 PRODUCTION AND IL2 RECEPTOR GENERATION IN AIDS AND ALTERED KINETICS OF GAMMA INTERFERON IN AIDS AND AIDS RELATED COMPLEX. R. Paganelli, MR Capobianchi, I. Mezzaroma, GP. D'Offizi, M. Cherchi, F.Aiuti. Dept. Clin. Immunology and Inst. of Virology _Univ."La Sapienza"_ Rome ITALY
We evaluated T lymphocytes, CD4+, CD8+ subsets, lymphoproliferative response, IL2 receptor expression, production of IL2 and gamma IFN in response to PHA in 16 patients with AIDS, 19 with AIDS-related complex (ARC) and 15 controls. 2 AIDS were children, 14/16 AIDS had O.I. and 3 K.S. Absolute deficiency of CD4+ cells was present in AIDS and in most ARC, with CD4/CD8 ratio 1 in all AIDS but only in 6/15 cases of ARC. The addition of 10 U/ml of rIL2 to the cultures did not restore lymphoproliferation. IL2 production in supernatant was absent in 87% of AIDS (mean levels 0.2U) but near normal in ARC (4.3 U/ml vs 5.9-5.1 U/ml in controls).IL2 receptor generation was greatly decreased in AIDS,but only slightly in ARC(22%vs50%of cells).Gamma IFN production was decreased in AIDS(mean 42U/ml)but not in ARC(528U/ml,normal range 100-3000U/ml) Kinetics analysis showed that some defective cases had delayed production,reaching normal levels at 72hrs of culture in 3/11AIDS and 5/7 ARC patients. None of the ARC patients developed O.I.after a follow up from 18 to 30 months.

TP.118 Increase of HLA antigen in the sera of patients with associated HIV infection disease
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An increase of beta 2 microglobulin in the sera of patients with AIDS or AIDS-related complex is well stablished but there is not quantitative data about soluble HLA molecules in such conditions. We studied the HLA antigen serum level in 14 patients with AIDS, 9 patients with AIDS related complex and 8 with lymphadenopathy syndrome; 33 HIV positive and 33 HIV negative sypmtomlese intravenous drug users were included as control. Of the 14 patients with AIDS 10 had opportunistic infections, two B cell neoplasia, one progressive leukoencephalopathy and one had Kapsi's sarcoma. The diagnosis was confirmed by the Spanish Commitee for AIDS.

The amount of HLA in the sera was quantified by the method described by Ferreira et al, using the mab W6/32 bound to micro ELISA plates and purified HLA molecules as standard. The results showed significative increase of HLA in patients with AIDS or AIDS related complex as compared with the observed in controls.

HLA (micg/ml)	HIVnegative i-v drug users	HIVpositive	LAS	ARC	AIDS
mean+SEM	5.95±3.45	7.92±3.15	9±3.76	12.3±4.1	19.2±5.9

TP.119 Reactivity of Patients' Sera with HTLV-III$_{RF}$ Env Gene Recombinant Antigens Expressed in Escherichia coli.
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The env gene from the HTLV-III$_{RF}$ strain, proviral clone λHAT-3, was engineered as a env-lacZ gene fusion in an E. coli expression vector. Various 5' and 3' deletions of the env sequences were isolated. The hybrid proteins synthesized by 11 separate fusions were characterized by Western blot analysis and ELISA tests using sera from infected patients. The results show that there are three immuno-dominant regions in these clones. One of these lies within codons 54-123 of the gp41 gene sequences. The two others map to the amino terminus and the carboxy terminus of the bacterially expressed gp120 gene sequences. The results with the gp120 recombinants show that hybrids carrying amino acids 30-182 or 483-520 are immunoreactive, while a hybrid with amino acids 182-462 is unreactive.

The systematic analysis of these types of families of hybrid proteins can help localize regions of immunological importance. This approach allows precise mapping of areas that may be important for clinical diagnostics or for vaccine development.

TP.120 In Vitro Studies of HTLV-III/LAV Tranemission from Monocyte/Macrophages to Autologous T Cells.
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It has been demonstrated in patients with lymphadenopathy or AIDS that, in addition to OKT4$^+$ T lymphocytes, cells of the mononuclear phagocyte series frequently harbor HTLV-III/LAV. The longevity and magnitude of virus expression in these kinds of celle indicate thet they represent a reservoir for virus dissemination and also play a role in the pathogenesis of the disease. Because there is close cooperation and interaction between cells of the mononuclear phagocyte series and T lymphocytes, we studied HTLV-III/LAV transmission from virus-infected monocyte/macrophages (MM) to autologous T cells using cocultivation methods. HTLV-III/LAV was efficiently transmitted into T cells within 10-20 minutes after cocultivation with the virus-infected MM cells. Compared to cell-free infection of T cells using culture fluids harvested from the same MM cultures which were used for the cocultivations, virus expression was detected earlier and virus production was significantly higher in the T cell cultures infected by cocultivation. These results suggest that efficient transmission in vivo from MM cells to T cells may occur.

TP.121 Deficiencies of Lymphocyte Proliferative Responses of HIV-Seropositive Men to HIV Antigens and Cytomegalovirus.
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Defects in the ability of lymphocytes to respond to antigens are characteristic of AIDS. We therefore tested proliferative lymphocyte responses from HIV-seronegative (HIV-) men, asymptomatic HIV-seropositive (HIV+) men and ARC or AIDS patients to purified HIV, recombinant envelope and core proteins of HIV, synthetic HIV envelope peptides and to CMV. Lymphocytes from HIV- and CMV- men did not proliferate in response to any of these antigens although recall responses to tetanus toxoid, Candida, or to PHA were detected. Only a small percentage (<10%) of HIV+ men regardless of clinical status showed significant ($p<0.001$) lymphocyte proliferation to any HIV antigens tested. All HIV- CMV+ men showed significant lymphocyte responses to CMV. In contrast, some HIV+ CMV+ asymptomatic men, many ARC, and all AIDS patients were hyporesponsive or anergic in their proliferative responses to CMV. Proliferative responses to CMV but not to any HIV antigens could be induced or augmented by the addition of recombinant IL2. These results indicate deficiencies in cell-mediated immunity to HIV and CMV including but not limited to IL2 deficiencies in individuals exposed to HIV. The mechanisms of this immunodeficiency including defects in antigen presentation and immunosuppression by HIV proteins will be discussed.

TP.122 Suppression of In Vitro Hematopoiesis Following Human Immunodeficiency Virus (HIV) Infection.
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Abnormalities including leukopenia, anemia, and thrombocytopenia are observed in patients with the acquired immunodeficiency syndrome (AIDS) or the AIDS-related complex (ARC). We examined the effects of two recombinant hematopoietins, human granulocyte/macrophage-colony stimulating factor (rGM-CSF) and recombinant erythropoietin (epo), on the in vitro growth of bone marrow progenitor cells from untreated AIDS or ARC patients. Bone marrow progenitor cells from all 10 patients in the study were responsive to rGM-CSF and epo when cultured in the presence or absence of normal human serum. Sera or purified immunoglobulin from AIDS or ARC patients, however, suppressed colony formation by bone marrow cells from AIDS or ARC patients but not from healthy individuals. Purified rabbit immunoglobulin to recombinant HIV envelope protein (gp120) reproduced the suppressive effects observed with immunoglobulin from HIV seropositive subjects. HIV could be recovered from pooled bone marrow progenitors from AIDS marrow when these progenitors were co-cultivated with normal peripheral blood mononuclear cells. Thus, it appears that antibody in the serum of individuals following infection with HIV may contribute to immune-mediated suppression of hematopoiesis in AIDS or ARC patients. In the absence of antibody, bone marrow progenitors may be infected with HIV but they respond normally in vitro to rGM-CSF and epo. Clinically, GM-CSF has been capable of eliciting a leukocytosis in AIDS patients. The extent of this leukocytosis, however, may be limited by the presence of antibody to HIV.

TP.123 Membrane Markers of Bone-Marrow Cells from AIDS Patients.

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		CD4		CD8	
Median % :		Periph.blood	Bone marrow	Periph.blood	Bone marrow
AIDS	N=8	15	20	35	22
Controls	N=7	41	26	23	13

The lymphocytes in peripheral blood (PB) represent only 1/1000 of all lymphocytes, the majority of which is found in the lymph nodes, the spleen, and in the bone marrow (BM). The lymph nodes in AIDS are depleted for CD4 cells and invaded by CD8 cells. We have investigated and compared the percentage of lymphocyte markers in bone marrow aspirates and peripheral blood from eight patients with AIDS and from seven controls (donors for BM transplantation). The analysis was made on a FACS analyzer and included both lymphocytes and monocytes/blasts. Only one of seven controls had a higher percentage of CD4 cells in BM (26%) than in PB (23%). Two of the AIDS patients had normal fractions of CD4 cells in PB (48% and 49%) and lower fractions in BM (33% and 43%). Of the six AIDS patients with decreased numbers of CD4 in PB, four had higher CD4 fractions in BM (PB/BM 7%/11%, 9%/18%, 22%/36%, 8%/22%), one had 11% in both PB and BM, and one had 18% in PB and only 3% in BM. The percentage of CD8 cells were increased in both PB and BM from AIDS patients compared to controls, but these cells did not dominate the BM. Two of the BM from AIDS patients were CD10 (Calla) positive (12% and 21%). The presence of CD10 positive blasts which are precursors of B cells, indicates an increased turnover and may reflect the polyclonal activation of B cells in AIDS. None of the cells inAIDS or control BM were IL-2 receptor positive, and the fractions of BM cells bearing HLA-DR, Ig, or CD16 (NK cells) were similar in patients and controls.(This work was supported by the Danish Cancer Society and the Danish Medical Council.)

TP.124 HLA A1, B8, DR3 as a Risk Factor for the Development of Clinical Sequelae to HIV Infection in the Edinburgh Haemophilia Cohort.

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Several reports have suggested that HLA antigens may influence the response to HIV infection. We have carried out a study of the distribution of serologically defined HLA antigens in a group of haemophiliacs. Thirty-two patients not previously exposed to HIV received a batch of locally produced FVIII contaminated with HIV; 18 became seropositive and 14 remain seronegative. In addition we have typed 28 other haemophiliacs not exposed to this batch; 6 are seropositive and 22 seronegative. Using a standard 2-stage complement-dependant microcytoxicity assay these patients have been typed for 17 alleles at the HLA-A locus, 32 private and 2 public alleles at the HLA-B locus and 8 alleles at the HLA-DR locus.

We found no significant association between any one HLA antigen and the risk of seroconversion following exposure to HIV. However the HLA antigens A1, B8 and to a lesser extent DR3 were over-represented in the subgroup who seroconverted. Among 7 patients with clinical progression following seroconversion (1 with AIDS, 3 with ARC, 2 with PGL and 1 with thrombocytopenia) the combination A1, B8 was present in 5, 4 of whom also carried DR3, the 5th not yet having been typed at the DR locus. The A1, B8 combination was found in only 2 of 13 seropositive patients without evidence of clinical progression. Neither patient has yet been typed at the DR locus. A1, B8 was present in 3 of 14 seronegative aptients exposed to the contaminated batch of factor VIII. One patient is DR3+; the DR type of the other two is not yet known.

TP.125 Molecular Analysis of Growth Factor(s) Produced by HTLV-II Transformed Cell Lines and Cell Clones Developed From Kaposi'Sarcoma (KS)

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Human T-cell Lymphotropic Virus Type II (HTLV-II) transformed CD4+ cell lines produce a strong growth stimulating factor(S) inducing KS-derived cell lines to proliferate. This factor(S) is heparin independent and stimulates preferentially KS cells, but it is also active on normal endothelial cells. Interleukin-1(IL-1) induces the proliferation of KS cells, but the mitogenic response plateaus earlier than the factor(S) from HTLV-II transformed cell line and IL-1 has a very low effect on normal cells. In contrast classical growth factors: e.g., human endothelial growth factor (ECGF) and fibroblast growth factor (FGF) induce proliferation of normal endothelial cells, but do not seem to stimulate KS cells. Molecular analysis confirmed the novelty of the factor(S) released by HTLV-II transformed cells. Parallel studies indicate that KS-derived cell clones also possess a growth factor specific for endothelial cells. The KS-derived cells contain abundant levels of mRNA which hybridize to probes derived from the FGF cDNA sequences. However, differences are evident by Northern blot analysis in the species of RNA expressed in these cells as compared to the messages found in human hepatoma cell lines and in bovine hypothalamus for FGF. The biological data and the molecular characteristics suggest that the factor produced may be FGF or a related protein. Further experiments may determine whether this factor has a role in an autocrine stimulation which leads to the abnormal cellular proliferation found in KS.

TP.126 Evidence for increased circulating T6 positive cells in ARC and AIDS patients.

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The circulating T6 bearing cells were analyzed in patients with HIV infection in order to investigate the T lymphocyte dysbalance. Monoclonal antibody of the COI class (IOT6) was used in an indirect assay using a goat antimouse bound colloidal gold immunoglobulin as second antibody. Patients were all seropositive for anti-HIV and were classified according to the CDC criteria. Controls were performed in healthy volunteers and patients suffering from viral hepatitis. Results are as follow :

T6 + cells		CONTROLS	AIDS	ARC	ASYMPTOMATIC	VIRAL HEPATITIS
	n	40	41	15	13	9
%	m	5,5	32,2	24,3	8,4	10,0
	S/√n	0,5	3,5	5,2	1,8	1,7
per µl	m	111	265	468	196	147
	S/√n	11	36	112	48	11

Variance analysis showed that the number of T6 positive cells was significantly increased in AIDS and ARC patients when compared to all other groups ($p < 10^{-3}$) as expressed in percent of total lymphocytes and in absolute number per µl of blood. There was no significant difference between controls, asymptomatics and patients with viral hepatitis. No correlation was found between the number of T6 and T4 positive cells or the T4/T8 ratio in all HIV positive patients. However a correlation could be evidenced between the percentages of T6 positive cells and the total lymphocyte counts per µl of blood ($n = 69$, $p < 10^{-3}$).

Since IOT6 monoclonal antibody is known to recognize T lymphocytes precursors, this increase of circulating IOT6 positive cells could be the consequence of the regeneration of T cells in these lymphopenic patients. Further studies are actually done to evaluate a possible pronostic value of this parameter.

TP.127 Normal antibody-dependent cellular cytotoxicity (ADCC) mediated by effector cells defective in natural killer (NK) cytotoxicity in patients with acquired immunodeficiency syndrome (AIDS).

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We have recently reported that the depressed NK cytotoxic activity in AIDS may be due to a defective "trigger" required for activation in the lethal hit stage of the NK lytic pathway. NK effector cells can mediate antibody dependent cellular cytotoxicity (ADCC) through the use of the FCγ receptor (FCγR). Therefore, it was important to delineate whether the defect in AIDS NK cells affected the ADCC activity observed by these cells. The ADCC cytotoxic activity of AIDS PBL was found to be within the normal range despite the absence of significant NK activity. Depletion of FCγR bearing cells resulted in elimination of both the ADCC and NK cytotoxic functions. The frequency of ADCC target conjugates and the frequency of killer cells from AIDS PBL were comparable to normal controls. Furthermore, the frequency of two-ADCC target cells killed by a single effector was comparable that of the controls. However, when mixture of NK and ADCC targets were used to form two-target hetroconjugates, the AIDS effector cells lysed only the bound ADCC target. Furthermore, AIDS effector cells stimulated with ADCC targets, but not with NK targets, were shown to release natural killer cytotoxic factors (NKCF), postulated mediator of the NK CMC reaction. These findings indicate that the NK/K cells in AIDS are triggered normally for ADCC activity but are not triggered for NK activity. Furthermore, the results indicate that the lytic pathway is not impaired in the AIDS NK/K cells. Supported by the AIDS Task Force and in part by the NCI tumor immunology training grant CA-09120.

TP.128 HIV Glycoprotein (gp120) Serves as Target for Antibody-Mediated Cytolysis.

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Patients infected with HIV produce antibodies against the major envelope glycoprotein gp120, which have been shown to exhibit virus neutralizing activity and may be involved in preventing further spread of the virus. Anti-gp120 antibodies in patient sera as well as sera from immunized animals show extensive cell surface reactivity against both virus infected cells and purified gp120 complexed with the CD4 molecule on uninfected lymphocytes. Such observations led to an investigation of whether these cytophilic antibodies could mediate the destruction of virus infected and/or antigen coated target cells.

Antibody-Dependent Complement-Mediated Cytolysis (ACC) was evaluated in a series of 90 minute ^{51}Cr releaae assays in which gp120-coated, normal $CD4^+$ lymphocyte targets were incubated with either patient sera or immune goat serum in the presence of rabbit complement. Although goat anti-gp120 serum directed the lysis of gp120 coated targets, none of the patient sera contained significant lytic activity. In contraat, patient sera, in combination with normal donor lymphocytes, effectively directed Antibody-Dependent Cellular Cytotoxicity (ADCC) of gp120 coated $CD4^+$ cells in 4 hour ^{51}Cr release assays. Goat anti-gp120 serum failed to mediate ADCC. The finding that patient sera can direct the cell mediated destruction of gp120 bearing cells indicates the presence of an additional barrier to HIV infection.

TP.129 The Immunopathology of Peripheral Nerve Disease in AIDS

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Peripheral neuropathy in AIDS is of unknown pathogenesis. In our series, histopathologic evidence of peripheral neuropathy with demyelination (78%), axonopathy (31%), or mononuclear cell inflammation (40%) was observed in 19 of 20 (95%) patients. Demyelination was patchy and associated with endoneurial fibrosis. Axonopathy was characterized by attenuation and fragmentation of fibers and axonal spheroid formation. Immunohistochemical staining demonstrated a 4.5-fold increase in the density of endoneurial mononuclear inflammatory cells relative to controls. 60% of the inflammatory cells were identified as Leu-4+ T lymphocytes or Leu-M3+ macrophages. The remaining 40% of mononuclear inflammatory cells, not identified immunohistochemically, were also probably macrophages based upon their cytomorphology. T8+ (cytotoxic/suppressor) cells predominated among the T lymphocyte subsets. B cells were not identified in the nerves. Diffuse immunostaining for HLA-DR was present on endothelial cells, mononuclear inflammatory cells, and Schwann cells, and variable patchy immunostaining for HLA-DR was present on nerve fibers. In contrast, control nerve specimens showed staining for HLA-DR limited to endothelial and a few scattered mononuclear cells. The findings suggest that the peripheral neuropathy of AIDS results from specific T cell and macrophage-mediated tissue destruction as occurs in viral infections.

TP.130 Human Monoclonal Antibodies Directed Against gag Gene Products of the Human Immunodeficiency Virus (HIV)

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Tonsillar B lymphocytes from a patient infected by the human immunodeficiency virus (HIV) were transformed with Epstein Barr virus obtained from the B95-8 marmoset cell line. Three cloned lymphoblastoid cell lines secreted human monoclonal antibodies that specifically reacted with HIV as detected by immunoblot analysis. The monoclonal antibodies recognized proteins of 55, 41 and 25 kd.

Serum antibody responses to the p55 gag precursor protein and the p25 core protein of HIV have been well documented. The reactivity of these human monoclonal antibodies suggests that individuals naturally infected with HIV also respond to a p41 gag gene product. This p41 protein is probably a processing intermediate generated from the p55 gag precursor. Caution should therefore be exercised when examining Western blot profiles and designating an anti-p41 response as anti-gp41. This report is the first description of a human monoclonal antibody directed against gag gene products of HIV. The effect of this newly identified human monoclonal antibody on viral replication will be discussed.

TP.131 Prognostic Importance of Presence of NAb and Anti-p17/24 Antibodies in HIV Infected Individuals.

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We have serially tested for antibodies directed against HIV antigens and for the presence of neutralizing antibody (NAb) activity in the sera of 149 prodromal homosexual males, 36 patients with AIDS, and 33 heterosexual males under double blind conditions in 1985-1986. Presence of anti-HIV antibodies was determined by ELISA and Western blot methods. All AIDS patients and 101 of 149 (67.8%) prodromals were found to be HIV (+). All heterosexual subjects and 48 of 149 (32%) prodromals were HIV (-). The neutralizing activity of the sera was tested by a newly-developed micro-culture assay system using H9-HIV susceptible cells. Study subjects were devided into NAb+ and NAb- groups. During the 18-months observation period, 2/80 (3%) HIV+ NAb+ prodromals progressed to AIDS and died, as compared to a significantly greater ratio, 5/21 (24%) of HIV+ NAb- prodromals whose conditions thus progressed. Similarly, among the NAb+ AIDS patients, 8/23 (35%) patients died, while 10/13 (77%) NAb- patients died from the disease. In both these groups, lack of neutralizing capacity in the serum, was directly related to rapid disease progression. In addition, absence of anti-p17 and p24 antibodies as well as the lack of the NAb appears to be closely related to clinical progression of the disease. These observations could be a useful tool in the clinical management of patients.

TP.132 Humoral and cellular responses to HIV and polypeptides in a model system.

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A model system was established for studies of humoral and cellular immunity to HIV antigens in primary and reactivated infection and after vaccination. Macaques (Macaca fascicularis) were immunized with purified HIV, a cell extract rich in gp120 or polypeptides of cloned genes for parts of p24, gp41 and gp120 (pE3). Western blots best showed the appearance of antibodies to nucleocapsid protein while antibodies to higher molecular weight envelope glycoproteins were better demonstrated by radioimmunoprecipitation. With whole HIV, antibodies to p24 appeared first, and sometimes were the only ones to be demonstrable. Several immunizations with HIV were required to obtain antibodies to gp120, and the response was weak. (g)p41 also had a poor immunizing effect. IgG synthesis from B-cells in vitro was well demonstrable to whole HIV, and generally paralleled the antibody titers of sera after multiple immunizations. The HIV-specific lymphocyte proliferation response as measured by DNA synthesis was best seen with p24, followed by (g)p41, pE3, gp120 and whole HIV.

TP.133 Interleukin 2 (IL2) Receptor Gene Expression in Human Monocytes Infected with Human Immunodeficiency Virus (HIV)

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Circulating monocytes recruited to sites of inflammation undergo phenotypic and functional changes characteristic of activated macrophages. We investigated the role of IL2 receptor expression in activated monocytes in vitro and then examined the effect of HIV infection in vitro and in vivo on monocyte IL2 receptor expression. We first demonstrated IL2 receptor gene expression and synthesis of the receptor in activated monocytes. The addition of recombinant IL2 to suboptimally activated IL2 receptor-positive monocytes enhanced both the production of reactive oxygen intermediates and cytotoxic activity and also regulated interleukin 1 (IL1) production. Normal monocytes cocultured with HIV in vitro also expressed increased surface receptors for IL2, and the addition of recombinant IL2 to these cells caused an increase in reverse transcriptase activity, suggesting that IL2:IL2 receptors may play a regulatory role in the infective process. We next examined the effect of HIV infection on IL2 receptor expression in monocytes from AIDS patients. Peripheral blood monocytes from patients with AIDS expressed increased levels of IL2 receptors as well as HLA-DR antigens. In addition, Northern blot and in situ hybridizations demonstrated an increase in the level of IL1 and IL2 receptor mRNAs in the circulating monocytes from these patients, indicating the prior in vivo activation of these cells. These studies suggest that HIV infection may contribute to the in vivo activation of monocytes in AIDS patients and that these activated cells may play an important role in the pathogenicity of the disease.

TP.134 Modulation of T Cell Proliferative Responses by Envelope and Core Antigens of the Human Immunedeficiency Virus.

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We studied the ability of the recombinant envelope protein, P121, and two synthetic core proteins, HGP-18 and HGP-30, to activate peripheral blood lymphocytes (PBL). P121 is a 82 amino acid peptide corresponding to the env-lor region of HIV. HGP-18 and HGP-30 are protein analogues that share 100% homology with the gag protein, P17, of HIV; HGP-30 also shares 50% homology with thymosin-alpha-1.

PBL from control and symptom-free subjects (SF), cultured for 5 days with each of these antigens, resulted in minimal proliferation (SI<5.0). The addition of HGP-30 to PBL cultures containing PHA did not appreciably affect proliferation. In contrast, HGP-18 added to PBL cultures containing PHA significantly augmented the PHA responses of SF($p=0.04$) but not of controls. Unlike the gag proteins, the envelope protein, P121, suppressed the PHA responses of both the SF and controls by 36.3% and 24.1%, respectively.

These results suggest that the gene products of HIV elicit different but specific host cellular immune responses. Experiments are in progress to study the mechanism of these interactions and to determine if these responses differ quantitatively or qualitatively from SF to more symptomatic individuals.

TP.135 Relationship Between Skin Test Reactivity and T4 Counts in Screened Human Immunodeficiency Virus (HIV) Seropositive Active Duty and Marine Corps Personnel

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OKT4-positive lymphocytes (T4 counts) and delayed hypersensitivity skin testing (DHS) are major parameters used in the staging and evaluation of HIV seropositive patients. We evaluated the relationship between T4 counts and DHS results in 600 patients identified by the HIV screening program mandated by the Department of Defense (DOD). The skin tests were applied by the Allergy Department at each hospital. Three hospitals used the Merieux multitest and one used intradermal injection of a panel of 5 antigens. For data comparison, normal is defined as reactivity to 2 or more antigens; hypoergic as reactivity to 1 antigen; and anergy as no skin test reactivity. Summary data is presented below.

T4 Counts	Skin Test Reactivity Results(%)			#Patient
	Anergic	Hypoergic	Normal	Evaluations
0-100	73	17	10	29
100-200	50	18	32	44
200-300	17	29	54	90
300-400	11	25	64	96
>400	13	21	66	418

Skin test reactivity remains stable down to T4 counts of 300, with a sharp decline in reactivity observed at counts below 200. Nevertheless, great individual variability is seen with 27% of HIV seropositive patients with T4 counts less than 100 still able to mount some skin test reactivity.

TP.136 EVIDENCE OF HUMAN IMMUNODEFICIENCY VIRUS ENCEPHALOPATHY IN THE ABSENCE OF OVERT NEUROLOGICAL DISEASE

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Twenty five HIV seropositive, male homosexuals with AIDS related complex (16) or AIDS (PCP within 90 days)(9) had neurological assessment upon entry into an antiviral protocol which excluded patients with overt CNS disease. Review of systems revealed complaints of memory loss and poor concentration (11), peripheral paresthesias (5), headaches (4), altered mood (4), and hallucinations (1). Abnormal recent memory and trail making tests were noted in 9 and 12 patients, respectively. Examination revealed a pathologically brisk jaw jerk and/or frontal release signs (13), hyperreflexia or asymmetric reflexes (12), postural tremor (10), incoordination (4) and diminished distal sensation (3). The neurological assessment was completely normal in only 4 patients.

CT scan revealed cortical atrophy in 4/6. MRI demonstrated diffuse hyperintense white matter lesions on T2 weighted images in 3/4. CSF examination in 16 patients disclosed a mononuclear pleocytosis (6-200 cells/mm^3) in 6, increased protein (46-79 mg%) in 7, and glucose 60 mg% in 12. CSF HIV cultures were positive in 4/7. Intrathecal synthesis of HIV specific IgG was detected in 11/14. All 14 had antibody to gp41, whereas only 6 had antibody to p24. No herpes viruses, adenoviruses or enteroviruses were isolated from the CSF.

Evidence of an underlying HIV encephalopathy in ARC and AIDS in the absence of readily identifiable neurological disease is extremely common. Over 80% exhibited abnormal neurological findings and 78% had intrathecal antibody synthesis to HIV. CSF studies and neuroimaging complemented the neurological examination in confirming the presence of HIV-related CNS abnormalities.

TP.137 Clinical Features of Transfusion-Associated Human Immunodeficiency Virus (HIV) Infections in Children. JOSEPH A. CHURCH, Childrens Hospital of Los Angeles and USC School of Medicine, Los Angeles, CA, USA.

Blood transfusion (tx) represents the risk factor in over 50% of HIV patients (pts) at Childrens Hospital of Los Angeles (CHLA). Of 17 pts (15 M, 2 F) with AIDS or documented HIV infection acquired through blood transfusions, 10 had AIDS, 5 AIDS-related disorders and 2 were asymptomatic. Ages at diagnosis (Dx) varied from 8 months to 4½ years (mean 3.7 years). Ten pts (9 M, 1 F) received Tx as premature infants; 5 other symptomatic pts (4 M, 1 F) received Tx at 2 days to 6 years of age. The 10 pts infected as prematures were compared to the 5 other symptomatic pts transfused later.

The time (in years) from Tx to development of symptoms (Sx) was 1.6 for prematures and 1.7 for the others, from Tx to Dx of AIDS or HIV infection was 2.7 and 2.8, respectively; and from first Sx to Dx 1.2 and 1.2, respectively.

Failure to thrive, chronic oral candidiasis and hepatomegaly were seen in both groups. Recurrent or persistent otitis media or sinusitis was seen in 9 of the prematures and 2 of the others. Interstitial pneumonias including P. carinii, lymphoid interstitial pneumonitis and pulmonary fibrosis were seen in 8 prematures and only 1 of the other pts. Four of 10 pts infected as prematures have died; 1 of 5 pts infected later has died.

In summary, Tx-associated HIV infection in premature infants was no more aggressive than that seen in pts transfused at older ages. The high prevalence of interstitial pulmonary disease in post-prematures may reflect microanatomic damage and/or local host defense disruption associated with the respiratory distress syndrome seen in these pts.

TP.138 Diagnosis and Investigation of Hairy Leukoplakia Using Non-Invasive Techniques

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A high proportion of HIV seropositive individuals with oral hairy leukoplakia (HL) subsequently develop AIDS. Diagnosis of oral hairy leukoplakia currently requires biopsy, a procedure which may not be readily available or may be contraindicated, for example in hemophiliacs. We have investigated the use of two non-invasive techniques directed towards establishing the presence of EBV in the epithelial cells of HL lesions. Filter in-situ hybridization (FISH) involved the use of the pBg12U probe for the IR-1 sequence of EBV, hybridized to cells obtained from smears applied to filters under suction, and visualized autoradiographically. Cytospin in-situ hybridization (CISH) involved the same probe, used on cells applied to glass slides by cytocentrifugation and visualized using a multistep biotin-enzyme technique. Twenty cases of biopsy-confirmed HL were studied to compare the ease and accuracy of FISH and CISH. Both techniques showed the presence of EBV-DNA in all cases. FISH showed very high sensitivity but was technically more demanding and involves the use of radioisotopes. CISH allowed identification of single positive cells, was quick and relatively simple. Both techniques permit confirmation of EBV infection in HL with high accuracy and may obviate the need for biopsy in some cases.

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TP.139 Evaluation of a Clinical Case Definition of Pediatric AIDS in Africa.

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To determine the accuracy of the clinical case definition for AIDS in children which was proposed at the second meeting of the WHO collaborating centers of AIDS December 1985, we examined and carried out HIV serology on all 155 children hospitalized at Mama Yemo Hospital between July 5 to 7, 1986. Nineteen (12%) of the 155 children examined were HIV(+). Symptoms and signs significantly associated with HIV seropositivity included: diarrhea lasting for at least one month, chronic or recurrent otitis (p=.03), generalized lymphadenopathy (p=.007), oral candidiasis (p=.03), hepatomegaly (p=.03) and splenomegaly (p=.02). Illness of the mother (p .0001) and presence of HIV associated symptoms or signs in the mother (p=.0001) were also strongly associated with HIV seropositivity. The provisional WHO clinical case definition of pediatric AIDS was found to have a specificity of 88 %, a sensitivity of 40%, and a positive predictive value for HIV infection of 30%.

Our study suggests that the use of the proposed WHO pediatric clinical case definition for surveillance of AIDS in African children will result in significant underreporting.

TP.140 Painful Sensory Neuropathy (PSN) in Patients with AIDS

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Paresthesias and dysesthesias confined to the feet are common symptoms in patients in the pre-terminal stages of AIDS. This clinical picture has been called PSN. Ten patients with those complaints were studied shortly before death. Examinations revealed elevated vibratory thresholds, increased sensitivity to pinprick, and reduced ankle reflexes. Electrodiagnostically, sural sensory responses were absent in 6 and reduced in amplitude in 4. Peroneal motor evoked amplitudes were absent in 2 and reduced in 8. Three demonstrated carpal tunnel entrapments, and ulnar sensory potential amplitudes were reduced in 4. Conduction velocities were normal or slightly reduced in proportion to the reductions in amplitude. EMG demonstrated acute denervation potentials confined to distal leg muscles. These studies are typical of a distal axonopathy.

In a retrospective study of AIDS autopsies, we previously reported four men with severe degeneration of the gracile tract of the spinal cord (Rance et al, Ann Neuro 1986, 20:146). All developed prominent distal paresthesias and dysesthesias, which increased in severity over 3-6 months. Vibration sensation was impaired in the feet, ankle jerks were depressed or absent, and plantar responses were flexor. In one, dorsal root ganglia revealed evidence of demyelination and remyelination with infiltrating lymphocytes and macrophages. No viral inclusions or perivascular inflammation were identified in the spinal cords.

The clinical and physiological picture of the 10 PSN patients and the character and distribution of the lesions in the gracile tract in 4 other patients with symptoms of PSN suggests a "dying back" process of the primary sensory axon. This may represent a degeneration in the dorsal root ganglion cells, possibly from direct HIV infection.

TP.141 Alterations in Sleep Architecture in Asymptomatic HIV Seropositive Patients

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HIV infection is associated with neurologic disease. Data on sleep are scarce and suggest that subjective complaints of initiating or maintaining sleep are secondary to anxiety or depression. No polysomnographic data exploring sleep architecture in HIV infected individuals exists.

A pilot study was conducted to evaluate sleep physiology in asymptomatic HIV seropositive patients. Eight HIV seropositive (western blot analysis)homosexual males (mean age of 37.6 years) (Group A) and 3 HIV seronegative homosexual men (mean age 28 years) (Group B) volunteered to complete a sleep history questionnaire and a polysomnogram (PSG). Both groups did not differ in their sexual practices or lifestyles. Two patients in Group A and none in Group B had sleep complaints,i.e. sleep onset and maintenance difficulty and daytime fatigue. Mean sleep efficiency index was less in Group A indicating a poorer quality of sleep (mean 87%,range 71-96%) compared to Group B (mean 94%, range 90-96%). Six of 8 Group A patients had above normal predicted percent slow wave sleep (%SWS) (mean 21.8%,range 16-32%),whereas this occurred in only 1 Group B patient. Also,%SWS in the second half of the night in Group A (mean 12.7%,range 2.2-25.1%) was greater than Group B (mean 5.3%,range 0-8.9%).

We hypothesize that sleep disturbances can be caused by altered biological processes and not just psychological factors. Early alterations in sleep architecture may be an early marker of CNS involvement in HIV infected patients.

TP.142 Is Cytomegalovirus (CMV) a cause of pneumonia in AIDS ?

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In order to investigate the incidence of CMV (frequency and prognosis) in the lungs of AIDS patients we examinated broncho alveolar lavage (BAL) fluid in 80 AIDS and 20 preAIDS patients observed during 14 months. BAL was performed either for pulmonary symptoms or unexplained fever (>3 weeks).

CMV was isolated by culture in 29 patients (32 BAL) and was the only microbiological agent in 14 BAL, and was associated with other agents in 18 BAL (14 Pneumocystis, 3 Mycobacterium avium intra cellulare (MAI), 1 Cryptococcus neoformans). 2 preAIDS patients had CMV in BAL and AIDS was diagnosed 6 months later in 1 of them admitted for an unexplained fever which was due to pericardial tuberculosis. CMV was observed in 13 AIDS having had at least one opportunistic infection (OI). It was also isolated in 14 AIDS during the first OI. 5/29 patients with CMV died of the pneumonia which required BAL, but no death seems to be specifically linked to CMV, since another agent was found in these cases: Pneumocystie (3), MAI (2) associated in 3 cases to pulmonary kaposi sarcoma. No patient died of pneumonia when CMV was the only microbiological agent.

CMV is frequently isolated in BAL during AIDS (30%). CMV seems to be isolated more often in advanced stages of the disease. The pathogenic significance of CMV is unclear in this disease.

TP.143 Increased Risk of Cervical and/or Vaginal Squamous Atypia in Women Infected with HIV.

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We studied women with AIDS as well as female sexual partners (SPs) of male AIDS patients to determine the prevalence of cervical and/or vaginal squamous atypia and its relationship to HIV infection. Subjects underwent standardized interviews regarding demographics and sexual history, complete physical exams including pelvic exam, and assay for HIV serum antibodies and T4 cell counts. Samples of cervical epithelium for cytologic evaluation were obtained and read by one cytopathologist blinded to the subject's HIV status. 35 HIV antibody + (HIV+) women (28 SPs and 7 with AIDS) and 23 without HIV infection (HIV-) (all SPs) were evaluated.

11/35 (31%) HIV+ subjects had evidence of squamous atypia compared with 1/23 (4%) of HIV- women (p=0.019). Compared to HIV- women, HIV+ women had a significantly increased frequency of venereal disease, decreased use of barrier contraceptives and fewer months since last sexual contact with an AIDS patient (p<0.05). HIV+ women also had significantly lower absolute T4 counts.

HIV+ women with atypia compared to HIV+ women without atypia had no significant differences with respect to any demographic, sexual or immunologic variables, except for more children among those with atypia (p<.05).

We conclude that HIV+ women have a significantly increased prevalence of cervical and/or vaginal squamous atypia compared to HIV- women. In the HIV+ group atypia was not associated with variables relating to sexual experience. Hypotheses to explain these findings include increased susceptibility of HIV+ women to agents which may potentially promote cervical or vaginal atypia (e.g. papillomavirus), a direct effect of HIV infection, or increased susceptibility of women with preexistent atypia to HIV infection. Additional epidemiologic, pathologic and virologic studies are required to explore these possibilities.

TP.144 Failure to Maintain Normal Growth Pattern in Pediatric Hemophilia: Possible Predictor of Progressive Immunodeficiency.

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Standard growth charts and clinical, serologic and immunologic measurements were carried out over 3 years (1983-85) on a cohort of 37 HIV-antibody positive hemophiliacs, aged 2-15. Seven patients (group A) failed to maintain a normal growth curve for at least 2 years, while 30 (group B) grew normally. The mean ages of group A and B were 11.5 years (range 2.8-15) and 8.1 years (range 2.5-14.9) respectively. All had previously used non-heat-treated concentrate and were HIV antibody positive by 1984. There was no significant difference between the amount of factor concentrate utilized by each group.

In 1983 there was no significant difference between the 2 groups in any of the immunologic or clinical parameters studied. By 1985 those who had failed to maintain a normal growth pattern had developed: 1) a significant decrease in the number and percentage of absolute T helper cells: 253/ul vs 813/ul, p<.01; 16.8% vs 30.4%, p<.01; 2) a decreased T helper/suppressor ratio: .37 vs .86, p<.01; and 3) decreased skin test reactivity. One patient who failed to grow has developed AIDS and 1 patient has had chronic diarrhea and weight loss; another has persistent oral candidiasis and recent severe weight loss. No patient in the control group is ill. Since those who failed to maintain a normal growth pattern exhibited significantly greater deterioration in immune studies than those who continued to grow and since cessation of normal growth often preceded laboratory or clinical deterioration, it is possible that a period of lack of growth could be predictive of more severe progression of clinical manifestations in children with HIV infection. It is also likely that growth failure is another sign of clinically symptomatic HIV infection in children.

TP.145 Evaluation of the WHO Case Definition of AIDS in Rural Zaire.

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The World Health Organization (WHO) has proposed a clinical case definition for AIDS for use in areas where medical facilities are inadequate to confirm AIDS as defined by the Centers For Disease Control. In these areas the clinical definition can only be evaluated against human immunodeficiency virus (HIV) antibody status; thie evaluation is therefore one of the case definition as an indication of symptomatic HIV infection.

Seventy-seven patients in 4 rural hospitals in the Equeteur Province of Zaire were examined and had sera tested for anti-HIV. Fulfillment of the clinical criteria was compared with anti-HIV status. Twenty-one (27%) patients were anti-HIV seropositive, and 22 (29%) fulfilled the criteria. For diagnosing symptomatic HIV infection, the WHO criteria performed as follows: sensitivity 52%; specificity 80%; positive predictive value 50%; negative predictive value 82%. The clinical spectrum of HIV infection is broad, and determining the amount of HIV related disease and deaths is more relevant in Africa than strictly defining AIDS. We propose the case definition be assessed accordingly.

TP.146 Examination of Neurodevelopmental Outcome in Congenital HIV Infection: Heterosexual vs. IVDA Transmission

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Previously described neurodevelopmental impairment in infants and children with AIDS includes a variety of cognitive deficits, motor delay, encephalopathy, acquired microcephaly, spasticity and dementia. Most cases of congenital AIDS to date have been traced to maternal IV drug abuse. Drug abuse during pregnancy is associated with greater fetal wastage and less favorable neurodevelopmental outcome in the newborn. A pilot study for a long term multidisciplinary prospective project was conducted to delineate those pernicious neurodevelopmental effects which were disease induced and those drug induced.

Sixteen HIV-antibody positive pediatric patients under the age of 2½ years were examined by raters blind to the etiology of the infection, using standardized cognitive measures and neurological assessment. A group of 10 were the offspring of confirmed maternal IV drug abusers; another 6 were infected in utero from heterosexual contact.

Statistical analysis using the Fisher exact test showed no significant differences between the 2 groups on either the neurological or cognitive (Bayley MDI scale) measures. Earlier onset of CNS symptoms was associated with a poorer long term developmental prognosis and a higher score on the AIDS embryopathy rating scale for related dysmorphic features.

Lack of significant differences between the groups suggests how severely the HIV infection affects the developing nervous system regardless of exposure to other potentially toxic environmental factors.

TP.147 Diarrhea in Patients with AIDS/ARC.

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Diarrhea is a common problem in patients with ARC and AIDS. Much time and effort is spent in evaluating these patients. We examined the records of 230 HIV antibody positive (53% AIDS; 47% ARC) patients. Of these, 64 (28%) had diarrhea and 63 were male homosexuals. Conventional work-up (stool smears and culture, ova and parasites, mycobacterial smear and culture, and viral culture) revealed causative organism(s) in 19 patients (29%). Eleven patients had infection with one and 8 with more than one organism. Thirteen different pathogens were recovered including Cryptosporidia (5), Giardia and CMV (4), Shigella flexneri (3), Entameba coli and Entameba hartmani (3), Isospora belli, Blastocystis hominis, E. histolytica, Salmonella typhi, Camphylobacter spp., and Pseudomonas putrefaciens (1). Seventeen of these 19 patients received specific therapy with 11 complete and 4 partial responses. Of the remaining 45 patients 22 (49%) had self-limited disease which required no therapy. Fifteen of these had ARC. Twelve others responded completely and 6 partially to non-specific anti-diarrhal agents (Imodium, lomotil). Only 5 patients had persistent diarrhea requiring further evaluation. Endoscopy and intestinal biopsy was diagnostic in 3 of 5 patients. Our data suggest that the majority of ARC/AIDS patients do not require endoscopy and intestinal biopsy for the evaluation of diarrhea since it is often self-limited or may respond to non-specific therapy.

TP.148 Renal Tubular Nephropathy in AIDS Causing Volume Depletion and Malnutrition.

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Weight loss and cachexia often accompany AIDS.We did renal clearance studies in 4 patients with AIDS,wt loss,cachexia and clear evidence of severe hypovolemia(postural hypotension,reflex tachycardia,high plasma renin and ADH levels, cvp 0),but no evident fluid losses. Renal tubular defects were shown in all pts by high renal excretion rates(RER) of uric acid(UA) and various amino acids(AA) despite low blood levels and volume depletion. Salt therapy did not correct volume depletion,but further increased RER of UA and AA,and showed abnormal RER for sodium,potassium and phosphorus. Also,one pt returned to baseline volume depleted state when extra salt was stopped. These data highlight the magnitude of the tubular defects since similarly volume depleted pts with normal tubular function markedly reduce RER and retain augmented salt intake. All pts had nl creatinine,urinalysis(no protein,glucose) and adrenal function. Opportunistic illnesses or drugs did not cause these effects. Conclusion: HIV infection appears to cause renal tubular defects which produce severe hypovolemia due to renal salt wasting,and also significant renal losses of other minerals and amino acids that worsen when replacing salt. Low plasma AA resulting from renal losses may partially account for the cachexia in AIDS. Salt therapy to replete volume given without other nutrients will aggravate malnutrition by increasing renal losses of amino acids and other nutrients.

TP.149 Distribution of HIV Message in Postmortem Brain

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The in situ hybridization technique has the potential for allowing very precise localization of the replicating human immunodeficiency virus (HIV) in the brains of AIDS patients who suffer from neurologic complications. We preliminarily tested the utility of this approach as applied to routinely fixed and processed tissues [Stoler et al (1986) JAMA 256: 2360] and here report additional studies of similarly processed brain tissue from autopsied AIDS patients. In this study we examined cases with, and cases without typical histopathological evidence of "AIDS encephalitis", but in either case with additional ongoing or potential complicating CNS pathology (eg. primary CNS lymphoma, systemic CMV infection). Our conclusions are: (1) that HIV can replicate in brain concurrently with other complicating CNS processes and (2) in situ hybridization applied to routinely processed autopsy (as well as surgical) tissue, provides the potential for direct study of the topographic distribution of HIV infection in brain, for correlation with specific neurologic impairment in life.

TP.150 Prognostic Indicators of Survival in AIDS Patients with Pneumocystis carinii Pneumonia: A Biostatistical Analysis

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In order to identify prognostic indicators of survival from Pneumocystis carinii pneumonia (PCP) we studied retrospectively our first 48 adult AIDS patients with PCP. We determined which clinical and laboratory features present early in the course of treatment were predictive of prolonged survival from an initial episode of PCP. Statistical evaluation of uncensored (followed to death) and censored (followed to date last seen) patients was accomplished using the survival analysis method of Kaplan and Meier. The Cox-Mantel test was used to determine whether the difference between separate Kaplan and Meier survival curves was significant.

Seven variables emerged as significantly associated with prolonged survival: an initial positive response to therapy, the presence of night sweats, a normal or near-normal chest Xray, an arterial oxygen tension $\geq$50mm Hg in room air, a TH/TS ratio $\geq$ 0.25, either no alteration of PCP therapy or alteration because of adverse reaction only and the absence of respiratory failure requiring artificial ventilatory support. The singlemost important indicator was the patient's initial response to anti-PCP therapy and emphasizes the importance of the clinician's assessment during the first 7 days in estimating the ultimate length of survival.

The presence of dyspnea on exertion and significant recent weight loss, a respiratory rate >30/min, fever, and a widened A-a gradient were associated with a general reduction in survival.

Familiarity with specific indicators of survival from PCP assists the physician in providing realistic information to the patient and his/her family regarding prognosis and guides decisions about future care.

TP.151 Neuromuscular Complications of Human Immunodeficiency Virus (HIV)

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We have seen the following neuromuscular complications in patients infected with HIV:

I. Peripheral Neuropathies of the following subtypes: a) Acute demyelinating inflammatory sensorimotor polyneuropathies identical in presentation and course to Guillain-Barre syndrome with occasional cytomegalovirus (CMV) inclusions in the Schwann cells; b) Mononeuropathy multiplex which can remit spontaneously or evolve into a distal symmetric polyneuropathy; c) Chronic, slowly progresive sensorimotor demyelinating polyneuropathy with CSF pleocytosis and elevated protein; d) Small fiber, distal, symmetric sensory neuropathy, due to a distal axonopathy; and e) Large fiber sensory ataxic neuropathy due to ganglioneuronitis. Nerve biopsy shows demyelination with inflammatory infiltrates (Ia, Ic), vasculitis (Ib), axonal loss (Id), inflammation in the ganglia (Ie), or a combination of findings.

II. Polymyositis as described (Dalakas et al. JAMA, 1986).

III. Type II muscle fiber atrophy, as the only morphological finding in the weak muscles due to poor nutrition, rapid weight loss or remote effet of lymphomas.

IV. Amyotrophic Lateral Sclerosis (ALS) in one case.

Although some neuropathies and the type II atrophy can be due to nutritional factors, there is evidence that the majority of the cases are due to HIV infection, co-infection with other viruses, i.e. CMV or due to immunopathologic mechanisms. Based on our experience, a neuromuscular disease may be the presenting sign of an ARC or developing AIDS or the only clinical manifestation of HIV seroconversion. Patients at risk who present with neuropathy or myopathy, should therefore be screened for HIV.

TP.152 The Control of HIV Transmission - A Public Health Challenge Requiring the Maximum of Foresight, Courage and Reassessment and Flexibility

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It is clear that, because most (>90%) HIV transmission in the United States is through behavior that can be modified, HIV transmission can be controlled. The marked behavior changes of San Francisco homosexual men and the resulting decreased infection rates attest to the potential success of behavior modification.

Yet, despite some local successes by-and-large our AIDS prevention efforts are failing. Why? First, our political, budgetary, and public health managenal systems are not geared to such long term emergencies and, as a result, have largely been paralyzed by the day-to-day chaos of AIDS. Second, we as a society have not developed the courage to move ahead with the difficult issues involved with fielding an AIDS prevention program.

With recent publications (Surgeon General's Report, NAS Report, Francis and Chin) there are prevention plans around which local programs can be designed. The message to be promulgated by these programs is rather simple: Dangerous virus - take personal responsibility to protect yourself: 1) If you are going to have sex, use a condom. 2) Don't use drugs; if you must, don't share unsterilized needles/syringes. 3) If you are going to get pregnant and possibly have been exposed, be tested before and if you are positive, don't become pregnant.

In the absence of effective vaccines or therapeutic agents, the extent of spread of HIV will be determined by the effectiveness of changing at-risk behavior. That effectiveness will require an immense short term "catch up" program of adult education, motivation and skill building followed by "maintenance" programs through schools and adult updates. In addition, prevention centers where individuals and families can find information, testing, and support groups will be increasingly important. Finally, assessment by periodically determining prevalence and incidence of infection, behavior changes and STD rates will be critical in evaluating the success or failure of the program so that appropriate changes can be instituted.

TP.153 HIV-1 and 2 are present in Ivory Coast in AIDS patients

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Investigation of AIDS in Ivory Coast showed that the disease became clinically evident by the end of 1985 and took epidemic proportions in 1986. Sera collected in June 1986 from patients with AIDS, according to the WHO Bangui definition, showed in 30 % of the cases antibodies to HIV-1 alone, in 20 % antibodies to HIV-2 and in 50 % antibodies to both HIV-1 and HIV-2 env and gag antigens. Sera considered as HIV-2 positive exhibited however weak and variable cross reactivities to HIV-1 gag products (p18, p26, p55). Survey of prostitutes in Abidjan showed that about half of them had antibodies to both HIV-1 and 2. These results indicate that both viruses are present in Ivory Coast, that they are associated with AIDS and that infection by one HIV strain does not protect from the other.

Prior sero-epidemiological investigation (Ouattara et al, Ann. Inst. Pasteur (Virology), 1986, 137E: 303-310) showed a low prevalence of infection by HIV-1 in the general population of northern, eastern, western and southern regions of Ivory Coast in mid-1985. Prevalence of HIV-2 antibodies in these sera is being investigated.

TP.154 Limited Value of Mycobacterial Smears in the Diagnosis of Pulmonary Tuberculosis in AIDS/ARC Patients.

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Tuberculosis (TB) is increasing in incidence in certain geographic areas where both TB and HIV infections are endemic. Prior studies have emphasized the presence of extrapulmonary disease in patients with both infections. Less well known is the fact that the majority of such patients have pulmonary TB as a component of multisystem tuberculous infection. We reviewed our experience with TB diagnosed by culture over a two year period from January 1, 1985 to December 31, 1986 at a metropolitan hospital in New York City serving East and Central Harlem and the South Bronx. Over this time period 104 hospitalized patients had pulmonary TB. Of these, 33 (32%) were known to have or develop AIDS (11) or ARC (22). Of these 33 patients 94% were male. Of the 71 patients with pulmonary TB without AIDS or ARC, 75% were male. Mycobacterial smears of pulmonary secretions were significantly less frequently positive in AIDS/ARC patients 16/33 (48%) (mean 2.5 sputum smears examined/patient range 1 to 9) compared to 54/71 (76%) in patients without AIDS/ARC ($p < .05$).

We conclude that about one third of pulmonary TB patients in certain areas of New York City have AIDS/ARC. The diagnosis of pulmonary TB should not be excluded on the basis of negative sputum smears. Empiric anti-TB treatment is warranted when TB is suspected in the AIDS/ARC patients pending culture results.

TP.155 AIDS-associated Kaposi's Sarcoma: Antiproliferative Effect of Recombinant Interferon Alpha.

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Twenty-eight patients with biopsy-proven Kaposi's sarcoma were treated with interferon alpha 2a. Daily intramuscular injections of 18×10^6 Units were given for 3 months, followed by 3-weekly administrations subsequently. Staging of patients was performed according to the Walter Reed classification: the number of patients is given in brackets: WR1 (0), WR2 (6), WR3 (3), WR4 (4), WR5 (11), and WR6 (4). Response to treatment was judged in monthly intervals. An antiproliferative effect of interferon was observed in 9 patients (32%) during the first 3 months of IFN substitution and remained so for at least 6-9 months. The median observation time of the responder group was 11.5 months. Three patients died 11, 15, 17 months after start of treatment due to opportunistic infections or tumor progression. All of them had a less favorable score in the WR classification (WR3-5). The majority of patients in the nonresponder group had a higher WR score (WR2 (1), WR4 (4), WR 5 (10), WR6 (4)). Most patients suffered from repeated episodes of opportunistic infections. Seven out of 18 died, the median observation period was 6 months, ranging from 2 to 18. Some patients achieved stabilization by the combined treatment of IFN together with vinblastin. Thus, patients with Kaposi's sarcoma and HIV infection classified according to WR into stage 2 or 3 may have a favorable response to interferon alpha 2a.

TP.156 Asymptomatic Myositis in HIV Antibody-positive Men

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Among the first 500 active-duty naval personnel identified as HIV antibody-positive and evaluated at the Naval Hospital, San Diego, 17 were noted to have creatine phosphokinase (CPK) levels more than 50% above the normal range for the hospital laboratory. All were asymptomatic with regard to musculoskeletal problems. After bed rest 4 of these individuals continued to have markedly elevated enzyme levels. CPK isoenzyme determination was 100% MM (skeletal muscle-related) in each case. Muscle strength testing and electromyography were normal in 3 men. Muscle biopsies of 3 of the 4 showed acute myositis. Only one of the 4 developed AIDS. His myositis regressed during treatment for PCP but recurred when his pneumonia recurred. Two others were in DoD (Walter Reed) Class 1 and the third in Class 3. These 3 have remained well, with persistent moderate-to-marked CPK elevations.

A recent paper reports acute symptomatic polymyositis in association with AIDS. It further implies that the use of steroids as therapy for myositis may enhance the onset of AIDS. We present these cases as the opposite end of what may be a spectrum of HIV-associated myositis. Only one of the 4 developed AIDS. He was not treated with steroids, but eventually died of AIDS. The remaining 3 show no evidence of progressive HIV-associated disease. Further study will be necessary to confirm an association between HIV and myositis in asymptomatic antibody-positive individuals.

TP.157 The cerebrospinal fluid diagnosis of HIV-encephalitis

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In order to establish a reliable procedure for the early diagnosis of HIV-encephalitis, 56 patients - 15 HIV-antibody positive, 10 with ARC and 31 with AIDS - were examined with the following methods that have been recently developed to evaluate the humoral immune response within the central nervous system:
- the quantitation of the locally produced immunoglobulin fractions in CSF (IgG, IgA and IgM) by an empirical differentation diagram.
- the comparative quantitation of HIV-specific antibody activity in CSF ans serum by a modified ELISA based on identical IgG-concentrations. This method avoids the calculation of indices and compensates impairments of the blood-CSF barrier.
- the confirmative evaluation of the HIV-specific antibody spectrum in CSF and serum by Western blot.

A CSF/serum ratio of the specific antibody activity above 2 is strongly suggestive for an intrathecal HIV-antibody synthesis. According to this criteria 46 % (7/15) HIV-antibody positive patients showed intrathecal antibody synthesis indicative of a very early HIV-infection of the central nervous system, whereas 70 % (7/10) of the patients with ARC and 65 % (20/31) of the patients with AIDS showed evidence for HIV-encephalitis. The local production of immunoglobulins, however, does not correlate to apparent neurological symptoms.

TP.158 Patterns of Magnetic Resonance Brain Scanning of Lesions in AIDS and ARC Patients.

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Magnetic resonance (MR) brain scans of 30 patients with either acquired immunodeficiency syndrome (AIDS) or AIDS-related complex (ARC) were reviewed. Twenty patients had focally abnormal neurological examinations at the time of scanning. Pathological diagnosis was available in nine. Four patterns of abnormality were observed on T2-weighted images. Multiple discrete high signal foci (Type A) were found in patients with toxoplasmosis and progressive multifocal leukoencephalopathy (PML). Large, bilateral patchy to confluent high signal areas within the white matter (Type B) represented a white matter encephalitis secondary to cytomegalovirus (CMV) or human immunodeficiency virus (HIV). Generalized enlargement of the cortical sulci and ventricles (Type C) reflect atrophic changes probably from the chronic HIV infection. Solitary high signal intensity lesions (Type D) suggested a focal (VZV and coccidioidomycosis in our series) opportunistic infection. Differential diagnosis of brain abnormalities in patients with AIDS can be assisted by recognition of these characteristic patterns.

TP.159 Central Nervous System Reactions to Trimethoprim-Sulfamethoxazole in Acquired Immunodeficiency Syndrome (AIDS) Patients.

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Adverse reactions to trimethoprim-sulfamethoxazole (TMP-SMZ) therapy, especially leukopenia, thrombocytopenia, and rash, occur with increased frequency in patients with AIDS. Only one CNS reaction (seizures) to TMP/SMZ in this population has been reported. The CNS side effects of TMP-SMZ reported in normals include headache, depression, and hallucinations. Three patients who had tremor as a prominent manifestation of TMP-SMZ therapy were observed in an 18-month period. One patient also developed hallucinations, another a wide-based gait and dysmetria. Two of the patients were noted to appear apathetic at the time of the reaction. Symptoms occurred 4-9 days after the onset of therapy and were co-incident with the development of leukopenia. All three patients had a mild hyponatremia (127-130). The tremor, hyponatremia, and leukopenia resolved after discontinuance of the TMP-SMZ with marked neurologic improvement evident in the first 24 to 48 hours. During this same interval 27 additional AIDS patients were treated with TMP-SMZ for Pneumocystis carinii pneumonia, 25 of whom were treated with both Pentamidine and TMP-SMZ, either concurrently or sequentially. Laboratory investigations failed to implicate alternative etiologies for the tremor. This experience suggests that not unlike the increased incidence of other toxicities previously reported, neurotoxicity to TMP-SMZ may be more frequent in the AIDS population than is generally appreciated.

TP.160 RETINAL DETACHMENT IN TREATED CYTOMEGALOVIRUS RETINITIS.

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Despite the frequent occurrence of cytomegalovirus (CMV) retinitis in AIDS patients, associated retinal detachment has not been reported. We treated twenty-five patients with AIDS and CMV retinitis with ganciclovir. Each patient was treated initially with 2.5 mg/kg every 8 hours for 10-20 days (induction) and then was placed on a maintenance regimen of 5 mg/kg/day 5-7 days/week. Every patient showed evidence by funduscopic exam of regression of the retinitis after the initial induction dosing. Ten eyes of six patients developed retinal detachment during maintenance ganciclovir treatment. Retinal detachments presented clinically as acute, sudden loss of vision in the affected eyes. Multiple breaks in areas of peripheral, healed, atrophic retina accounted for the detachments. All eight eyes undergoing surgery had extensive retinal detachments that were reattached with vitrectomy and silicone oil. In the fellow eye of one patient, laser treatment was used prophylactically to wall off a peripheral patch of healed retinitis. Endoretinal biopsies and culture were taken in five eyes; evidence of persistent CMV was seen in two cases despite concurrent and clinically effective ganciclovir therapy. We conclude that retinal detachment is a frequent complication of treated CMV retinitis. These detachments are often surgically correctable. Because of the propensity of these eyes to develop proliferative vitreoretinopathy, vitrectomy and the use of silicone oil may offer long-acting tamponade to the extensive areas containing retinal breaks as well as preventing potential future retinal breaks in zones of healed retinitis. The possible effectiveness of laser prophylaxis to surround areas of thin healed retina warrants further evaluation.

TP.161 Prevalence of hairy leukoplakia and oral candidiasis among HIV-infected Danish hemophiliacs.

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Oral hairy leukoplakia (HL) and candidiasis occur frequently and early among seropos. homosexuals but are largely undescribed among hemophiliacs. All known patients with severe hemophilia (90) in Eastern Denmark were invited for oral examination. Seventyseven (85%) responded, and the oral examination was conducted without knowledge of the HIV-antibody status. Of the 77 patients 42 (55%) were seropos..Only one had AIDS.

Erythematous (atrophic) oral candidiasis was found in 4 seropos. (10%) and in one seroneg. patient (3%). No cases of pseudomembranous candidiasis were seen. HL was found in 6 seropos. patients (14%) and in no seroneg. patients. Among the 6 HL patients 1 had AIDS with PCP and 1 non-diagnosed lung symptoms. The mean T-helper:T-suppressor cell ratio of the HL patients was 0.3 whereas tha same ratio was 1.0 for the 36 seropos. non-HL patients ($p=0.0013$). The mean number of T-helper cells was 0.2×10^9 and 0.8×10^9 among the HL and non-HL seropos. patients, respectively ($p=0.0001$). Thus, seropos. hemophiliacs with HL have more impaired immune system than seropos. hemophiliacs without HL. The observed prevalence rates appear to be lower than those so far reported among seropos. homosexuals. The prognostic significance of these findings has to be elucidated.

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TP.162 Routine Blood Cultures in AIDS Patients.

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Blood cultures (BCs) for bacteria are commonly drawn in the febrile AIDS patient (pt) despite the relative infrequency of bacteremia versus opportunistic and non-bacterial infections. This observation prompted an analysis of the utility of BCs for 'routine' bacterial pathogens in AIDS patients.

The charts of 65 of the 68 pts with AIDS followed at the Cleveland Clinic from 1981 through 1986 were available for review with attention to the number of positive and negative BCs, presence of central venous catheters, clinical diagnoses, and pt outcome. A total of 710 BCs for aerobic and anaerobic bacteria were drawn on 60 patients. Only 13 episodes of bacteremia were detected, and 5 of these were due to staphylococcal infections of central venous catheters. The remaining 8 episodes were primarily due to gram-negative bacilli from various sources: E. coli urosepsis, K. oxytoca pneumonitis, K. oxytoca biliary sepsis, E. coli of unknown source, and S. pneumoniae pneumonia. Two pts had polymicrobial bacteremia (due to paratracheal abscess and to sinusitis).

Non-catheter related bacteremia was seen in pts with far-advanced AIDS, always occuring several months after diagnosis (mean 358 days, range 169-898 days). Gram-negative bacteremia usually signified terminal disease with only one of 6 pts surviving beyond one month (mean 17 days, range 1-65 days). These data suggest that routine bacterial BCs in AIDS pts are of low yield except in the presence of central venous catheters or far-advanced disease.

TP.163 Prognostic factors for Pneumocystis carinii pneumonia requiring mechanical ventilation.

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Mechanical ventilation (MV) has been reported to be associated with a poor prognosis in Pneumocystis carinii pneumonia (PCP). Records of 19 patients (pts) requiring MV in association with their first episode of PCP were analyzed. Group A (GA) consisted of 8 pts who survived; group B (GB) of 11 pts who died. The mean ±SD of the duration of symptoms was 13±10 days and 23±19 days for GA and GB respectively ($p=.03$). Arterial oxygenation deteriorated and A-a gradient widened more precipitously in GA. The time from diagnostic bronchoscopy to initiation of MV was 1.5±0.5 days and 6±7 days for GA and GB respectively ($p=.001$). MV was necessary for 6±4 (range 1-6)days in GA and 19±16 (range 6-60) days in GB pts. Admission and peak serum LDH concentrations were similar in the 2 groups. However, LDH decreased by at least 40% from the peak level in all pts in GA by 5 days after intubation while it fell in only 4 of 11 GB pts. Concomitant early infections were seen in 3 pts of GA (1 S. epid. sepsis, 1 salmonella sepsis and 1 mycobacterial isolate from the sputum) and in 7 pts in GB (3 S. aureus sepsis,4 S. aureus pneumonia and 2 mycobacterial sputum) ($p<.05$).

We conclude that 42% of pts with PCP may recover from required MV. Factors associated with recovery include short duration of symptoms prior to admission, need for intubation shortly after bronchoscopy, early improvement in serum LDH levels and the absence of concomitant bacterial infections.

TP.164 Muco-cutaneous Manifestations in HIV Positive Subjects

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We studied the muco-cutaneous lesions in 310 HIV positive patients attending our AIDS screening Centre. Two hundred seventy-seven were homosexuals, 30 were intravenous drug abusers, 3 were heterosexual males. Fifty-four were asymptomatic carriers (Walter Reed 1), 137 had persistent generalized lymphadenopathy (WR 2), 98 had ARC (WR 3,4,5) and 11 had full blown AIDS (WR 5K,6). Among this group 93 patients (30%) had mucocutaneous lesions. We considered 3 main categories: infective, tumoral and other. Morphological, histological, immunohistochemical and electronmicroscopic studies were performed.

Viral infections were caused by herpes virus in 30 patients (9,67%), human papilloma virus in 20 (6,45%) and by both viruses in 10 patients with Oral Hairy Leukoplakia (3,22%). Only 3 patients were affected by bacterial folliculitis. Oral thrush was present in 12 subjects (3,82%) while other dermatomycosis were found in 7 subjects (2,15%). Five patients (1,61%) had muco-cutaneous Kaposi's Sarcoma.

An important role was played by Seborroehic Dermatitis that was present in 26 patients (9,38%) often with widespread lesions resistant to therapy. We also observed subjects with Yellow Nail Syndrome, Immune Complex Vasculitis, severe Psoriasis.

Some of the skin diseases we observed had a strong relation to the clinical stage of immune-depression; five out of 12 patients with oral thrush also had Candida Esophagitys and 5 out of 10 patients with Oral Hairy Leukoplakia developed full blown AIDS within the year.

TP.165 Pneumocystis Carinii Pneumonia (PCP) : value of Pulmonary Function Tests (PFT) follow up.

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Among 52 AIDS patients (pts) admitted from 7/84 to 9/86 with BAL proved 1st episode of PCP, 19 were followed up by serial PFT over a mean period of 10.2 ± 4.2 months. Tests were : transfert lung capacity for carbon monoxide (TLCO) ($N \geqslant 80\%$ of the predicted value by steady state method, corrected for anemia) and alveolar arterial gradient for partial pressure of oxygen ($A - a)O_2$ ($N \leqslant$ 20 torrs). PCP relapse occured in 6/19 patients. None of them had specific maintenance therapy.

At the time of 1st PCP, PFT revealed significantly low TLCO (49.8 ± 12.5) and major hypoxemia ($A - a)O_2$ = 41.4 ± 13.7). In all 19 cases, PFT values 1, 2 and(5 ± 1)months after 1st PCP episod were subnormal(TLCO = 85.6 ± 21 ($A - a)O_2$ = 16.9 ± 9.64); with no significant difference between patients with/ without relapse.

Relapse was suggested within 8.8 ± 1.6 months after 1st PCP by sudden decrease in TLCO (53.75 ± 5.85) and severe hypoxemia (40.2 ± 11.7) in the six pts. Three of them had no radiological changes at that time. TLCO and ($A - a)O_2$ one month later were 68.5 ± 20.9 ; 22.6 ± 9.5).

PFT follow up in these pts showed : 1) normalisation of both TLCO and ($A - a)O_2$ one, two and five months after 1st PCP, and no predictive value for PCP relapse ; 2) sudden deterioration preceeding X Ray changes in 3/6 cases, at the time of relapse ; 3) More severe changes in TLCO and ($A - a)O_2$ one month after relapse/one month after 1st PCP.

TP.166 Chemoprophylaxis Prevents Recurrence of Pneumocystis carinii Pneumonia (PCP) in Retrovirus Induced Immunodeficiency (AIDS)

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Fifteen patients with biopsy proven PCP and HIV induced immunodeficiency (AIDS) were evaluated. After recovery from the initial episode of PCP, two patients received no chemoprophylaxis while 13 patients received chemoprophylaxis with either one tablet weekly of pyrimethamine-aulfadoxine (FAN), or one tablet trimethoprim-aulfamethoxazole 80mg/400mg twice daily (TMP-SXT). Recurrence of biopsy proven PCP was noted in both patients who did not recieve chemoprophylaxis, 4 and 8 months after original PCP episode. These two patients were subsequently placed on chemoprophylaxis after their second episode of PCP. No patient (0/15) recieving prophylaxis redeveloped PCP. Six of fifteen died during follow up period (mean time to death 10.3 months, range 2-31 months). Three of these six had post mortem examination; none had histological evidence of PCP. Nine of fifteen still survive (mean follow up 13.7 months, range 6-22 months). Chemoprophylaxis was highly effective in preventing recurrence of PCP ($p < 0.001$). Although both regimens were effective in preventing recurrent PCP, a trend toward increased mortality was suggested in the TMP-SXT group. In the FAN regimen group there were 1 death/104 man months of follow up as compared to the TMP-SXT group with 5 deaths/91 man months of follow up ($p=0.07$). A placebo-controlled trial is currently in progress to determine the efficacy of FAN chemoprophylaxis prior to the initial episode of PCP in Walter Reed stage 5 and 6 patients.

TP.167 Esophageal Candidiasis in High-Risk Patients for AIDS.

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Esophageal candidiasis may be asymptomatic and not associated with oral thrush.To evaluate its prevalence in high-risk groups for AIDS we endoscoped 50 patients(45 intravenous drug addicts and 5 homosexuals)through 1986.None had oral thrush or esophageal symptoms.Forty had generalized lymphadenopathy.None fulfilled AIDS criteria at admission.All but 2 had antibodies to HIV detected by ELISA method.In 9 of them esophagoscopy showed plaques of white exudate,scattered in some.Cytologic examination of esophageal brushings demonstrated candidiasis in all them.Biopsy was positive only in 2 cases probably because of sampling error in dealing with scattered foci of fungal involvement.In these 2 cases biopsy showed only moderate,not invasive,esophagitis.One out of nine was negative for HIV antibodies.Patients with esophageal candidiasis have been admitted because of idiopathic thrombocytopenic purpura in 2,right-sided endocarditis in 2(in 1 associated also to a pulmonary tuberculosis),constitutional disease(group IV,subgroup A)in 2 and gonococcal sepsis,pneumonia and left arm cellulitis in the rest.The median T4/T8 ratio in this group was 0.55(range 0.13 to 1.13).The follow-up during this year has not shown the evolution to AIDS.In 2 cases(1 of them with positive biopsy)we demonstrated,by esophagoscopy,spontaneous resolution without treatment at 10 days interval.The other patients received a 10 days course of oral ketoconazol.Asymptomatic candida infection of the esophagus is not an uncommon disease in patients at risk for AIDS,it may disappear spontaneously, is not associated with unfavorable outcome and should not be considered a criterion for AIDS unless shown clearly invasive by biopsy.

TP.168 Serum Adenosine Deaminase Level; A Simple Screening test for Disseminated Mycobacterial Disease in Patients Seropositive for Human Immunodeficiency Virus

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Adenosine Deaminase (ADA), an enzyme of purine metabolism, is produced by activated T-lymphocytes and plays an important role in T-cell maturation. Surprisingly, this enzyme has been reported to be normal in the T-lymphocytes and high in the null lymphocytes of patients with the Acquired Immune Deficiency Syndrome (AIDS). We measured the serum levels of ADA in 32 hospitalized patients with positive serology for Human Immunodeficiency Virus (HIV) and 33 age matched control subjects (hospital personnel). ADA was analyzed by the standard Giusti and Galanti colorimetric method. Among the seropositive patients, 12 had Pneumocystis carinii pneumonia, 13 had mycobacterial disease (9 with histologic or culture proven disseminated disease and 4 with pulmonary tuberculosis), 2 had Kaposi's sarcoma and 5 met the criteria for AIDS related complex. The mean serum ADA was 74.78 IU/L (range 64.1-103.1) among the patients with disseminated mycobacterial disease; 72.7 IU/L (range 27.9-102.7) among the patients with pulmonary tuberculosis; 38.9 IU/L (range 17.1-56.1) among the 19 HIV seropositive patients without mycobacterial disease and 21.8 IU/L (range 11.9-42.6) among the healthy control subjects. The ADA level among the HIV seropositive patients with mycobacterial disease was significantly greater than that of the HIV seropositive patients without mycobacterial disease ($p<.0001$) and also greater than that of the healthy subjects ($p<.0001$).

Measurement of serum ADA is a simple test which may prove clinically useful in screening for the presence of disseminated mycobacterial disease among patients seropositive for HIV.

TP.169 Splenomegaly and Extrapulmonary Disseminated Pneumocystis carinii Infections in Patients with AIDS

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We studied the clinical course, surgical and autopsy pathology of 2 patients with AIDS who developed pulmonary and extrapulmonary disseminated infections caused by Pneumocystis carinii.

Patient 1: A 32 year old white male homosexual with left upper quadrant pain had splenomegaly and inguinal lymphadenopathy and was HIV sero-positive. He became febrile and an abdominal CT scan revealed focal defects in the spleen. At splenectomy, the spleen weighed 2000 grams and contained grey-white nodules; microscopic examination revealed foci of eosinophilic foamy necrosis containing cysts of P. carinii. He died 1 month later and autopsy revealed necrotic foci containing P. carinii in lymph nodes, liver, kidneys, ureter, jejunum, omentum, mesentery, appendices epiploicae, pancreas, adrenals, heart, thyroid, bone marrow, choroid and lung.

Patient 2: A 48 year old white male homosexual with fever, cough and progressive dyspnea was bronchoscoped and P. carinii pneumonia was diagnosed. He was HIV sero-positive and died 6 days later. At autopsy there was a 250 gram spleen containing white nodules and microscopic examination revealed P. carinii in spleen, lymph nodes and lung.

Although infection with P. carinii is typically confined to alveoli of the lung, in the immunodeficient host it may disseminate. The patients in this report developed splenomegaly as part of their disseminated extrapulmonary P. carinii infections. Clinicians and pathologists should be aware that P. carinii may infect organs other than the lung.

TP.170 Congestive Cardiomyopathy in Association with Acquired Immune Deficiency Syndrome in Children

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At autopsy in 5 children with AIDS, dilated cardiomyopathy characterized by a) enlargement of heart with biventricular dilatation, b) rare foci of myocardial necrosis with minimal to mild inflammatory infiltrate, c) hypertrophy, d) interstitial edema and myxoid change, 3) mild focal interstitial fibrosis, f) vacuolation due to fatty change, g) focal pericardial inflammatory infiltrate and h) endocardial fibrosis was seen. Two of the patients had developed congestive heart failure. Candidiasis, Aspergillosis, CMV or M. avium intracellulare infection was present in one patient each; mild focal calcification of small branches of coronaries without luminal narrowing was present in one patient and noneof the patients received any drugs commonly associated with hypersensitivity reactions. These factors are unlikely to be related to pathogenesis. Anemia, nutritional deficiency, infection and undetermined type and immunologic factors may play a role in the pathogenesis of cardiomyopathy in these children.

TP.171 Factors Distinguishing Homosexual Males Practicing Safe and Risky Sex

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A longitudinal study of patterns of sexual behavior among asymptomatic, homosexual males (N=161) in New York City was conducted. Participants were interviewed at two time points six months apart. Based on their reports of sexual behaviors during a recent "typical" month, respondents were classified at each time point as engaging in safe (or low risk) sex versus risky sex (e.g., unprotected anal intercourse or oral-anal contact).

Discriminant analysis was employed to distinguish the 48 males classified as safe at both T1 and T2 from the 58 males classified as risky in both periods. Statistically significant discrimination (Wilks' lambda = .675) was parsimoniously achieved through the use of seven predictor variables: drug use during or in anticipation of sexual activity; living with lover; number of years engaged in regular sexual intercourse with males; perceived emotional support; fewer friends or acquaintances with AIDS; self-esteem; and alcohol use. Of the predictors, drug use within sexual contexts is particularly noteworthy, since it provided the greatest relative contribution to the discriminant function and appears to be an important candidate for educational intervention.

Among the variables which did not significantly contribute to this discriminant function were: gay network affiliation, denial of AIDS threat and comfort negotiating sexual limits.

The significance of these findings for public health efforts will be discussed.

TP.172 A National Survey of Public Concern Regarding AIDS

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A survey on acquired immunodeficiency syndrome (AIDS) was conducted using a national random sample of 1,256 adults; the poll utilized random digit dialing and achieved 70% participation. Those with higher levels of education (at least a high school diploma vs. those without diploma) were somewhat more optimistic that AIDS would be under control five years from now (48% vs. 40%) and less pessimistic that AIDS would become a major epidemic (12% vs. 21%). Although only 10% of the sample perceived themselves at any risk of catching AIDS, 41% reported taking special precautions to avoid catching the disease. Perceptions of risk were highest among college graduates (16%), those aged 30-39 (16%), and those living in the East (16%). Blacks (61%) and Hispanics (58%) were more likely to report special precautions than were whites (37%). Of the total sample, 79% agreed either strongly (47%) or somewhat (32%) that the government should spend whatever it takes to find a cure or vaccine. Seventy percent of the total agreed either strongly (50%) or somewhat (20%) that the government should impose restrictions on gay bars and bath houses during the epidemic; there were educational differences on this issue, with 77% endorsement among those with high school or less, dropping to 62% for those with at least some college. Highest endorsement (97%, 88% strongly and 9% somewhat agreeing) was given to the proposal that individuals should take extra care in sexual relations and personal preventive habits.

TP.173 AIDS and the College Campus: A model Prevention Program

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Approximately 12 million students are enrolled in colleges and universities in the United States, representing about 5% of the population. In California alone, between 9,000 to 45,000 students currently enrolled in institutions of higher education can be expected to develop AIDS or ARC.

Upon entering college, the sexual networks of young people suddenly expand and experimentation with a variety of sexual practices, including bi-sexuality is common. A significant number of students also drink alcohol excessively and engage in recreational drug use. This leads to impaired judgment regarding sexual behavior and responsibility. For the most part, the threat of AIDS and death does not seem real to college students who believe themselves invincible.

The purpose of the poster session is to present a model for campus-based AIDS prevention. The model was developed and tested at the University of California, Berkeley in 1986-87. The State of California Department of Health Services contracted with Berkeley to design and disseminate this model. It is currently being replicated at other institutions of higher education. The poster session will highlight theoretical principals of AIDS education for this target group, with an emphasis on community organization and peer education. A 60 page training manual for campus AIDS educators wil be showcased along with institutional guidelines for policy development.

TP.174 Determinants and Effects of HIV Antibody Test Disclosure.

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The role of HIV antibody screening of high-risk groups is an unresolved public health issue. This study identifies the differences between individuals who choose to know vs. not to know their results and explores the impact of knowledge of HIV antibody test results on subsequent behavior. In a longitudinal study of initially asymptomatic homosexual/bisexual men (N=290) at a Boston community health center, 23% of the participants chose not to know their initial test result during the following six months. Antibody positive and negative men were equally likely to be informed. Multivariate analysis determined that the following variables were associated with the decision not to be informed: greater perceived severity of AIDS, lower reported effort to change sexual behavior, greater exposure to informational activities, and age 25-29. Significant differences were found by antibody status and test disclosure in emotional reactions (anger and depression) during the six months following test disclosure. Both emotional reactions and correlates of the decision to be informed should be considered in interpretation of subsequent behavior.

TP.175 Campaign to Promote Safe Sexual Practices in the Montreal Homosexual Population - Quebec

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With an AIDS community group (C-SAM) we developed a program to promote safe sexual practices among Montreal's homosexual population. Focus groups were used to review educational materials and extensive coverage by various gay media was provided. During a one week educational campaign, ten thousand health education pamphlets on "Safe Sex" and the same number of condoms were distributed in 27 gay bars and clubs, and 5 saunas by 30 trained health promotion volunteers.

A month later, a self-administered questionnaire was distributed in six representative establishments. The response rate was: 77.9%. Of the 839 respondents 79.3% had heard about the campaign and 50.9% had read the campaign pamphlet. Of those who read the pamphlet, 57.1% thought it had influenced their sexual behaviour. 45% of those who reported the campaign had an influence on their behaviour reported condom use compared to 19.6% of those who denied an influence of the campaign ($X2=49.03$, $p<0.001$).

18.9% of those who denied influence could not identify passive anal intercourse without a condom as high risk while only 10.8% of those reporting influence could not.

This project shows the feasability of a community preventive intervention in a population at high risk for AIDS.

TP.176 "AIDS Community Outreach for Intravenous Drug Users" Harvey W. Feldman, Ph.D. & Patrick Biernacki, Ph.D. YES Project, 1779 Haight St., San Francisco, CA 94117.

In May 1986, a community health education/outreach program was created in San Francisco to stop the spread of AIDS among intravenous drug users (IVDUs). Currently, the program employs eight workers who provide AIDS education, counseling and referral to drug users in those areas of the city that contain the highest concentrations of IVDUs. This paper describes and analyzes the major stages undergone since the program's inception and addresses problems encountered. The analysis will help other communities to develop similar outreach efforts.

The program developed in the following stages: 1) Formation of the overall strategy guiding the program effort toward the major goal of stopping the spread of AIDS among IVDUs; 2) Ethnographic studies of target areas to map out & analyze the needle-using scenes and drug-using practices; 3) Recruitment & training of an outreach staff component; 4) Successful entree into the target community; 5) Development & distribution of health promotion materials, condoms and small bottles of bleach; 6) Use of indigenous field assistants, who are natural leaders, to help promote safe health practices; 7) Utilization and management of the media to promote the project's goals; 8) Evaluation and reassessment of project plan and ensuring compliance with health messages, & 9) Entry into new IVDU scenes, when and how to move beyond the original target groups.

An administrative project evaluation indicates that, contrary to popular wisdom, IVDUs will change their behavior, especially in relation to sanitizing their shooting paraphernalia.

TP.177 Utilization of HIV Alternate Testing Sites in Upstate New York

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In June and July, 1985, the New York State Department of Health established HIV Counseling and Testing sites throughout New York State exclusive of New York City. Between June, 1985, and October, 1986, 7,608 persons received pretest counseling at the sites. Just over 69% of those being counseled elected to have the HIV antibody test (N=5,283). Of the 5,161 persons receiving posttest counseling during the 17 month period, 13% were positive via ELISA and Western Blot for HIV.

Individuals submitting blood for HIV testing were asked to voluntarily complete a questionnaire assessing demographic and HIV associated variables. Of the 2,788 (53%) completing the questionnaire 70% were males. The ages ranged from less than 15 to greater than 55 with 89% falling in the 15 to 44 year age group. The preponderance of those using the alternate site considered themselves to be white (84%). Of the 1,833 who considered themselves to be a member of a risk group: 44% were homosexual; 21% were bisexual, and 24% reported IV drug use. The two most common reasons for wanting to be tested were risk group membership and sexual contact with a risk group member. Nearly 80% considered themselves physically well at the time of testing.

TP.178 HIV Antibody Testing and Community Mental Health: Qualitative Outcomes of a Collaborative Model

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Despite near universal opposition by the gay community in April 1985 to AIDS antibody testing the Gay and Lesbian Counseling Service (GLCS) took a pro-active stance, working with the state Department of Public Health to design and implement a network of alternative testing sites. We describe the rationale for that decision and outcomes of two years of participation.

By participating in program design GLCS fostered principles fundamental to the Massachusetts program: (1) total anonymity, (2) an emphasis on education, especially about risk reduction, rather than on testing, and (3) access to a network of AIDS-aware medical and mental health providers sensitive to issues specific to high risk populations.

A key contractor with the Department in staffing/supervising several sites, GLCS also created and maintains a statewide provider referral list. Within its service region, GLCS provides both acute and long-term mental health services to test site clients withut regard for their ability to pay.

The changing composition and issues of test site clients forecast trends in service needs. GLCS flexibly responded to program needs by: (1) adding a voluntary (anonymous) second follow-up visit several weeks after individuals testing positive learn their status, for further help with referrals; (2) creating a "Safer Sex Psychoeductional Group" for ATS clients and others in the community; (3) sponsoring a support/educational group for pregnant women at risk through needle sharing or a sexual partner who has shared needles.

Other needs identified concern links between drug/alcohol use and unsafe sex, specific issues for bisexual men in long-term relationhips with women, and short- and long-term adverse sequelae of learning one's antibody status.

TP.179 The Alternative Test Site (ATS) in Rhode Island

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An ATS was established at the RIDH in June, 1985, to provide anonymous testing and counseling for Human Immunodeficiency Virus (HIV) infection to persons who might otherwise have gone to blood donation centers to be tested. As of January 28, 1987, 862 persons had attended. Median age was 31 years; 644 (75%) were male. 835 (97%) persons had their blood tested, 794 (95%) of whom belonged to groups at high risk for HIV infection. 406 (63%) males cited homosexual activity as a risk factor, and 116 (53%) women cited sexual contact with a high-risk individual.

HIV infection was confirmed in 74 (9%) persons; 71 (96%) belonged to high-risk groups. 65 (88%) were male, of whom 55 (85%) were homo/bisexual and seven (11%) were intravenous drug abusers (IVDA). Five (56%) women were IVDA, three (33%) were sexual partners of IVDA.

Among non-infected persons, 139 (54%) seen at the ATS from July through December, 1985, would have donated blood to determine their HIV antibody status if the ATS had not been available, while only 106 (40%) seen from July through December, 1986, would have done so (X^2 test for trend=10.2, p=0.0014). 23 (31%) infected persons would have donated blood.

The ATS in RI serves a population at high risk for HIV infection and plays an important role in monitoring HIV seroprevalence in this population. It has also served to divert infected potential donors from blood donation centers.

TP.180 Attitudes towards HIV antibody testing among General Practitioners.

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In order to evaluate the use of HIV antibody testing by general practitioners (GPs), a specific questionnaire was set up on the French Communicable Diseases Network in November 1986. This network, established in 1984 for the surveillance of certain communicable diseases, links 250 sentinel general practitioners (SGPs), by electronic mail to a central computer. These GPs were asked to report all prescriptions made for HIV antibody testing and to provide, for each case, the following information : person requesting test (i.e. patient or GP), reason for test, characteristics of patient, result of test and diagnostic method(s) used.

After one month of the study, preliminary results indicate that 14% (36/250) SGPs had prescribed at least once a test for a total of 65 subjects. The overall percentage of patients spontaneously asking for the test was roughly 50%. However this percentage was higher in male homosexuals (69%) than in IV drug users (33%), demonstrating the striking difference in the attitude in these two groups. Thirteen subjects were anti HIV positive, 7 of these being IV drug users.

Routine collection of information will provide further data on GPs' attitudes towards HIV testing, characteristics of tested subjects and help in adapting educational programs devoted to health care professionals.

TP.181 JUNIOR AND SENIOR HIGH SCHOOL STUDENT'S KNOWLEDGE ABOUT AIDS: THEY WANT TO LEARN MORE AND WANT TO LEARN IT AT SCHOOL

STEVEN D. HELGERSON, and the AIDS Education Study Groups, Yale University Department of Epidemiology and the Connecticut State Department of Health Services, including William Sabella.

We assessed knowledge about AIDS from 657 junior and senior high school students randomly selected from required English classes in two Connecticut school districts. Although many students had some factual knowledge about the virus that causes AIDS, many students were misinformed about methods of viral transmission, high risk groups for developing AIDS, and methods to avoid acquisition of the virus. Importantly, 58% did not recognize the existence of an asymptomatic carrier state; and 63% and 59% respectively did not recognize the potential for vertical transmission from fathers or mothers infected by I.V. drug use. Responses from students of different grades, ages, sexes, races and school districts, differed rarely and without apparent pattern. Students reported they had learned about AIDS mostly from television or radio (57%) or magazines or newspapers (16%); while few had learned from persons with whom they had frequent contact, such as parents (6%) or teachers (4%). Seventy-four percent of students said they wanted to learn more about AIDS, and 49% said they wanted to learn it in school. We conclude that students' knowledge about AIDS is not adequate, students wish to learn more, and information about AIDS should be presented in public schools.

TP.182 The AIDS/STD EDUCATION PLAN - An Innovative, Effective and Cost Efficient Program for Schools to Teach AIDS Education and Achieve the USPHS 1990 STD Education Objective

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The AIDS/STD EDUCATION PLAN is a response to the Surgeon General's Report on AIDS and to the USPHS 1990 STD Education Objective which encourage educators to teach students AIDS and STD education.

The AIDS/STD EDUCATION PLAN is a teacher training program based on the Educator's Guide to AIDS and STD's, a behavioral approach to teaching AIDS and STD education in a communicable disease conceptual framework, which is easily implemented in all schools.

Over 2450 educators who teach over 700,000 students in 3 states use the AIDS/STD EDUCATION PLAN.

Educators (N= 520) Evaluation Data:

Objective: (% educators responding "agree"):			
. offered effective methods and materials to teach students how to:		. made STD's easier to teach	(98%)
- recognize symptoms	(100%)	. produced significant educational gains in students':	
- find, use clinics	(90%)	- knowledge	(98%)
- refer sex partners for medical care	(89%)	- attitudes	(81%)
- follow treatment instructions	(93%)	- behavioral intentions	(77%)
- avoid STD's	(97%)	. will use the Guide again	(99%)

The AIDS/STD EDUCATION PLAN is cost efficient. Ohio achieved the 1990 STD Education Objective for less than 7¢ per students.

The AIDS/STD EDUCATION PLAN offers a prototype for schools to teach AIDS education and achieve the 1990 STD Education Objective at the city, state or national level.

TP.183 Lessons of History: An Examination of the US Army Pre-Antibiotic Venereal Disease Control Program and its Application to HIV.

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The venereal disease control program instituted by the United States Army in 1911 contained the following elements: Monthly lectures by medical officers about human reproductive physiology, the transmission and course of venereal diseases and an explanation of why sexual intercourse was not necessary to a healthy body, commanding officers expounding on the duty to remain healthy, chemical prophylaxis within two hours after fornicating, chaperoned social activities on Post, and pay withheld while in treatment.

The Army applied this program to every command on every Post in every part of the world where there were soldiers. The full program was applied regardless of variations in local circumstances and regardless of the ethnic, educational or cultural background of the troops. This Army wide program does appear to have caused a slow, progressive decrease in the venereal disease rate in the Army as a whole, but the reduction of the rate varied enormously with racial, geographic, and cultural factors.

History has for us an important lesson. A single massive aggressive intense repetitive educational campaign to control the spread of HIV in the United States will not be effective in stopping the HIV epidemic, and will slow it only modestly. There must be a campaign of a thousand parts, each directed towards a specific racial, economic, intellectual, social, political group and addressing specifically the issues critical to that group's sexual behavior. We need a rapid, rigorous rethinking of our educational programs and other efforts.

TP.184 Sharing of Paraphernalia in Intravenous Drug Users (IVDU): Knowledge of AIDS is Incomplete and Doesn't Affect Behavior.

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Transmission (T) of HIV among IVDU in the U.S. is occurring rapidly. Efforts at reducing this spread have been ineffectual. The potential for heterosexual and vertical T by this population is enormous. To determine causes of rapid spread we examined knowledge and behavior of 200 IVDU attending Sacramento(S) drug abuse clinics. Most addicts believed that: HIV was present in IVDU in S (90%); they would eventually acquire HIV if they continued sharing paraphernalia (P) (93%); HIV can be transmitted heterosexually (91%), vertically (100%); condoms can prevent sexual T (64%). 95% wanted to avoid acquiring HIV. With respect to behavior last time they shot up, however: 75% used own P, but 77% shared it; 87% cleaned P between users, but only with water, rarely disinfectant; majority (70%) had potential disinfectant solution readily available (bleach 35%, rubbing alcohol 56%, peroxide 31%, wine 23%). Addicts expressed: surprise at rate of HIV spread; ignorance of potential disinfecting agents, methods for cleaning P; reluctance to carry P because of criminal possession laws; strong desire to continue sharing P.

We conclude: some knowledge of HIV epidemiology exists among IVDU; IVDU are not aware of imminent risk of infection; knowledge of disinfection is dismal, rarely acted upon; sharing is likely to continue because of social aspects, criminal possession statutes. Immediate intervention, emphasizing AIDS risk, practical P disinfection methods and condom use is warranted. Failure to effectively intervene will result in rapid heterosexual and vertical T of HIV from this population.

TP.185 Follow-up to Ensure Counseling of HIV-Ab Positive Volunteers to HIV Test Sites (HTS)

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Confidential post-test counseling of volunteers for HIV-Ab testing gives positive persons an opportunity to learn their antibody status and receive personalized instruction on methods to prevent HIV transmission. Subsequent practice of safer sex and no needle share behaviors should reduce community transmission of HIV. Confidential (non-anonymous) testing and reporting allows public health follow-up of positives who fail to return for test results and counseling. Public Health can ensure (with provider consent) knowledge of test results and appropriate counseling for positive individuals. During 1986, 109 HIV-Ab positive individuals for whom there was no record of post-test counseling were followed by the Colorado Department of Health. The results were; 20 (19%) were brought to counseling, 33 (30%) had been previously counseled, 47 (43%) were not located, and 9 (8%) refused test results and counseling. Follow-up revealed that 82 (75%) positives provided accurate locating information at the time of test, but the proportion located and counseled decreased as the time interval between test and follow-up increased. Assuming that without counseling, each positive would transmit to 1 other individual, and that 40% of HIV-infected individuals experience some serious HIV-related morbidity, 20 new HIV infections, 8 of which may have developed AIDS or ARC, may have been prevented through this activity. Confidential testing and reporting, coupled with rapid and active follow-up of uninformed seropositives by public health can affect counseling and help reduce community transmission of HIV.

TP.186 AIDS Knowledge in Urban vs Rural Washington State High School Students.

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We surveyed 11th-grade students to assess AIDS knowledge as a basis for curricula development and to compare urban and rural students. Of 502 students surveyed, 214 were from urban King County (pop. 1,350,000; 300 AIDS cases); 288 were from rural Clallam County (pop. 52,000; 1 AIDS case).

Practically all students (96%) identified blood and semen as likely to spread HIV, but 39% thought saliva a likely source. Students recognized male homosexuals and IV drug users as risk groups, yet 48% thought female homosexuals at high risk. One in 5 thought living in the same household as someone with AIDS was risky, 32% thought AIDS could be acquired while donating blood; 27% thought mosquito bites a transmission source. Responses to individual knowledge questions varied little between urban and rural students. When the 2 groups were compared for percent correct responses on 34 knowledge questions, there was no difference (72% vs 74% correct). Significantly more urban than rural students wanted to know more about AIDS (70% vs 55%).

We concluded: 1) Both urban and rural students have basic knowledge of AIDS 2) The same misconceptions were prevalent in both groups 3) Rural students may not feel the need for AIDS education as acutely as urban students 4) One curricula is suitable for both urban and rural Washington State students.

TP.187 Prevalence of Antibodies to HIV in Prostitutes and Dominican and Haitian Cane Cutters in the Dominican Republic.

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In recent months,10 female prostitutes have returned to the Dominican Republic from neighboring islands and their seropositivity to HIV confirmed at the National Laboratory of the Public Health Ministry.

To examine the extent of AIDS seropositvity in resident Dominican prostitutes and heterosexual rural agricultural workers known to associate with prostitutes, two studies were undertaken using commercial ELISA kits and immunofluorescence or Western blot to reconfirm.

One hundred thirty nine prostitutes in Santo Domingo were questioned and bled. Two individual were seropositive. No correlation was found with kind and extent of sexual activity, VD, or relations with non-Dominicans.

Two hundred cane cutters of Dominican or Haitian origin residing within a 20 km radius were studied. Although they work in the same fields, these men live in separate areas, depending on nationality. The same female prostitutes, though, do intermingle with both groups. The health of the Haitians was considerably better than the Dominicans, using AIDS symptoms as criteria. More Dominicans reported venereal diseases. Nevertheless, 2 Haitians and no Dominicans were seropositive. No significant factor could be found to explain the seropositivity in these two. It is therefore assumed that they were infected through heterosexual sex in the Dominican Republic or Haiti.

These results indicate that heterosexual transmission from local prostitutes does not represent a serious threat now, but the international trade could provide a way for HIV to enter the rural and urban heterosexual population.

TP.188 Perceived Changes in Sexual Practices Among Homosexual Men

OON JOHNSON and H. M. MCGRATH, The University of Texas Health Science Center at San Antonio, TX.

The study surveyed 343 gay men in three Texas cities regarding their sexual practices during the last 30 days of this year (current sexual practices) compared with their sexual practices the same 30 day period one year ago (past sexual practices). The survey consisted of 16 items regarding current sexual practices and the same 16 items regarding past sexual practices. Behaviors were rated from 0 (low risk) to 5 (high risk). The mean scores of each current sexual practice were compared to each past practice using the Wilcoxon Matched-Pairs Signed-Ranks Test. Results indicate that the present sexual practices compared to past sexual practices are significantly less risky for contracting AIDS. Significant differences were found in the following high risk behaviors: anal receptive sex ($Z = -4.1969$ $p = <0.0000$); anal insertive ($Z = -4.9605$ $p = <0.0000$); oral receptive ($Z = -5.0503$ $p = <0.0000$); oral insertive ($Z = -5.2322$ $p = <0.0000$); location of meeting partners ($Z = -5.9669$ $p = <0.0000$); rimming ($Z = -4.7041$ $p = <0.0000$); swallowing of semen ($Z = -7.8294$ $p = <0.0000$); use of intravenous drugs ($Z = -14.3138$ $p = <0.0000$) number of sexual partners ($Z = -6.9269$ $p = <0.0000$); anonymous sexual partners ($Z = -6.0697$ $p = <0.0000$); sharing of anal sex toys ($Z = -2.8571$ $p = <0.0043$).

Although there are significant differences between current and past sexual practices, the study shows that 25.1% (N = 85) are continuing to have anal receptive sex without the use of condoms and 38.8% (N = 132) had two or more sexual partners within the last thirty days; and 24.4% (N = 83) had anonymous sexual partners.

TP.189 The Minnesota AIDS Media Campaign Consortium (MAMCC) - An Inter-organizational Approach

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During 1986, the Minnesota Department of Health developed a statewide health education and risk reduction plan to control transmission of HIV in Minnesota. One objective of the plan was to develop a statewide mass media campaign and to evaluate its success. In February, 1986 the Minnesota Poll, (a random statewide telephone survey) demonstrated that 90% of those surveyed considered mass media to be their primary source of AIDS information. To ensure statewide coordination of media efforts, the efficient mobilization of resources and the development of the most effective messages, we developed the MAMCC. The MAMCC is represented by two state public agencies (MN Dept. of Health, Dept. of Human Services), four local public health agencies (Hennepin Co. Community Health Dept., Mpls. Health Dept., Ramsey Co. Health Dept., St. Paul Div. of Public Health), three state and national private non-profit agencies, (MN AIDS Project, MN Medical Assoc., American Red Cross - St. Paul) and one private for-profit agency (MN Insurance Information Center). Marketing data from the statewide MN Poll, the Ctr. for Health Statistics, the MN AIDS Project surveys of youth and gay men guided the development of effective messages. Messages that have been developed promote the elimination of risk and utilization of services. A Twin Cities communications firm was selected in a competitive process to develop a creative strategic plan and media products for the media campaign. The MAMCC development, the ad agency selection process, the strategic plan, the media products and the evaluation techniques may have application value for other low prevalence states.

TP.190 AIDS: What You Need to Know: A Teaching Unit for Secondary Schools.

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We developed an AIDS curriculum to enable high school students to make informed decisions about AIDS as a public health issue and to make safer choices in risk-taking behavior. The curriculum covers AIDS epidemiology and projections, etiology, pathogenesis, blood-testing, and prevention.

The curriculum can be modified to suit the teaching situation. Depending upon the level of student knowledge and classroom constraints, any of the modules may be used. Assessment of student comprehension can be accomplished with evaluation modules consisting of learning-check questions and an exam for measuring objective learning.

We tested the curriculum on 240 eleventh graders. The test results revealed a significant increase in student knowledge, which corresponded with a positive change in students' attitudes about the disease. We conclude that exposure to a curriculum which impacts upon knowledge and attitude will enable young people to make informed public health decisions about AIDS.

TP.191 Distribution of Free Condoms as a Technique to Improve Acceptance of Condom Use.

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A survey was conducted to identify factors that might discourage the use of condoms. Respondents frequently cited interference with sensation, lack of familiarity and embarassment when purchasing condoms as important reasons for not trying them. A majority were not familiar with proper use of condoms, and personnel in STD clinics were rarely trained regarding procedures for proper application and use.

A graphic, pictorial brochure with step-by-step instructions for condom use was developed. A sample packet, including the brochure, safer sex information and condom samples was designed, labeled "A Healthy Gift from HERO." Gay-patronized retailers such as bookstores and gift shops were solicited to distribute these with customer purchases. Additional samples were prepared in a matchbook-cover package design, with the message "Stop Transmission Fluid Leaks" or "Life Preserver" imprinted on the cover.

Each of the sample packets were well received, and proved popular with both retailers and the general public. Samples became sought after, and proved to be an incentive, attracting targeted at-risk individuals to neighborhood educational presentations in order to obtain condom samples.

TP.192 Contact Tracing for STD's : A Review

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Contact tracing is an integral part of the standard public health approach to the control of sexually transmitted diseases (STD'S). It needs to be considered in the control of AIDS but can only be objectively evaluated when its definition and history are examined. Three distinct types of contact tracing exist. First, 'formal contact tracing' is a system in which specially trained staff interview patients, obtain names and addresses of sexual partners, locate these partners, and offer them examination and treatment. This is the traditional method used for gonorrhea and syphilis. Second, 'simplified contact tracing' refers to a variety of methods by which patients identify, locate and insure the examination of their own sexual partners without specifically naming them to the health worker. Last, 'conditional contracting' is a system in which contact information is given to the interviewer in trust and the patient contracts to notify these partners within a specified period of time. If this fails, the interviewer must seek out the sexual partner for assessment. All of these methods have clear advantages and disadvantages. Simplified contact tracing is the method usually used for AIDS and HIV seropositivity.

W. L. Munson in 1932 was the first to demonstrate that contact tracing was possible and effective in finding new infectious cases of syphilis. This 'sole-leather epidemiology' works as well for gonorrhea and has contributed significantly to the control of both.

TP.193 The blood donor perspective on false positive test results: The impact of anti-HIV test procedures

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For confirmation of initial findings on ELISA tests a fresh blood sample is needed, and the donor has to be called back. Of over 97,000 donations tested since May '85, 64 (0.076%) turned out to be false positive. With focused interview technique donors (n=30) were asked whether they associated the recall with AIDS or the anti-HIV test, how they handled the information about the test procedure, and what their reactions and feelings were.

Results: 19 Indicated to be upset by the recall. The thought of AIDS was mentioned by 17 although immediately rejected as considered impossible for themselves. Only 2 associated the recall with the anti-HIV test and 20 were ignorant of the existance of the test. 18 Indicated to pay hardly any attention to information related with AIDS because they have no risk factors. Ignorance of which tests actually are done made 16 upset by the thought of leukemia and cancer. 13 Associated the recall with their health at the moment of donation, and another 13 were very surprised by the recall because they felt healthy. 20 Indicated to consider blood screening as a very important check on their health.

Conclusion: Misunderstanding and anxiety can be relieved by carefully informing donors about meaning and content of donor screening. Information about important and new aspects of AIDS and screening procedures should preferably be included in this general information, rather than be given separate attention.

TP.194 Assessment of the AIDS Public Information Campaign in the UK

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The UK AIDS Public Information Campaign has involved newspaper and magazine advertisements,cinema, radio, street posters, TV and a leaflet delivered to all households. A detailed leaflet and telephone advice services have also been made available. This campaign has been subject to a larger programme of research than any other government-run publicity campaign.

In general, this research has shown (1) there was great interest in the subject of AIDS, with high percentages claiming to have seen and taken note of AIDS publicity, (2) the main methods of transmitting HIV were widely understood (3) misconceptions, for example as to the dangers of blood donation and transfusion and of casual contact were widespread but diminished over the time of study (4) any claimed recent changes in behaviour were in the desired direction, (5) offence was not caused by the material presented, in spite of mention of matters such as anal sex and drug injecting, (6) there was extensive support for a government-conducted campaign of this sort.

TP.195 Intravenous Drug Abusers Infected with Human Immunodeficiency Virus: Details of Behavioural Patterns over the Period of an Epidemic

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Intravenous drug abusers infected with AIDS virus and those apparently non infected were part of a cohort of 250 individuals followed over a 2 year period. Retrospective data was available on 117 individuals 683 men (71%) 34 women (29%) with a duration of heroin use of 3.6 years (SD 2.28, range 0.2-14.8). Importantly the length of time of intravenous drug use to presentation to medical intervention was 1.25 years (SD 1.43, range 0-7.75). The group had been in contact with the doctors for 12.8 years (SD 8.4+, range 0.1-28.6).

Case record search and detailed interview data was used to validate and corroborate the information as well as the subjective analysis of physicians with clinical responsibility.

Results demonstrate a peak of heroin use in 1981-1983, 60% of study group commencing use during these years. Subsequent heroin use was subdivided into Abstinent, Dependent and Non-Dependent use, most individuals demonstrating change between these patterns of behaviour every 0.48 years. As expected the total number of episodes correlated with duration of use ($r=0.425$, $p< 0.001$).

In the total of 4995 months of heroin use 39% was spent in abstinence, 10% in non-dependent and 48% dependent use. No correlation between groups and HIV seropositivity was demonstrated.

Conclusion: Drug users demonstrate varying patterns of use amongst individuals over time and in a group.

TP.196 Intergrating Positive Attitudes and Healing with the Expression of Painful Emotions and Dying in a Client Support Group

JIM GEARY, Executive Director, Shanti Project

In facilitating a support group for people with AIDS/ARC group leaders and members often find themselves in conflict regarding some members' desire to maintain a positive attitude and other members need to express depression, grief and/or concerns regarding dying. These needs can also be present concurrently in any one individual. Often members will not return to group because they find the group process too depressing or positive to the point where they feel unable to deal with difficult emotions.

Having facilitated a group for people with AIDS/ARC for 5 years, I have learned ways to support certain group members in maintaining a positive attitude, while assisting others dealing with painful emotions. These methods have resulted in a more intergrated approach to facing one's illness. I have found that when people realize that they can express strong emotions, yet still maintain an overall positiveness that this empowers them to handle whatever emotions they feel, rather than be controlled my them.

I have concluded by the success of my support group, measured in terms of longevity of attending members, that both metaphysical as well as more commonlly accepted approaches to dealing with illness can be combined and mutually supported for the benefit of everyone.

TP.197 Men With Isolated Thrombocytopenic Purpura - The Impact of Psycho-Physiological Intervention on Platelet Count

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A psychophysiological intervention composed of relaxation, imagery and therapeutic touch was investigated as to its effect on platelet count, helper: suppressor ratio, and adrenal function, in eight males with Isolated Thrombocytopenic Purpura. Individuals in the experimental group received a sixty minute psychophysiological intervention thrice weekly supplemented by an audiotape three times per day. After the five week intervention period participants used the audiotape alone. In a delayed start design, control group patients also received the intervention. This paper reports the psychological findings and their relationship to hematological and immunogical status. Control group patients exhibited an increase in tension and depression as measured by the Profile of Mood States from the baseline measures to the time of intervention. This same pattern was not observed in the experimental group. The experimental patients who showed decreases in tension, depression, anger, confusion and fatigue in the first five weeks exhibited further gains in the next five weeks. A trend was observed between decreases in depression and tension and an increase in platelet counts in two patients. Only one of the eight individuals had a normal H:S ratio. Increases and decreases in these ratios over the ten weeks were not remarkable. Five of the eight men had adrenal responses requiring further evaluation.

TP.198 Delivery of Psychosocial Services in a non-urban area using a model of Volunteer Efforts.

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AIDS Health-care experts generally agree that volunteer-based psychosocial support programs such as Gay Men's Health Crisis in New York and Shanti Project in San Francisco can deliver services in a highly cost-efficient and successful manner. However, such programs have been instituted primarily in urban areas. Hyacinth Foundation is one of the few programs operating in a suburban/rural setting as well as in urban centers. This paper describes the different issues that face service providers in suburban areas including such topics as: 1) dealing with geographic distances and the need for decentralized programs; 2) handling the generally greater stigma and shame that suburban AIDS patients feel and the concammitant need for extreme confidentiality, even secrecy, that these patients require; dealing with families of origin of AIDS patients in suburbia. We will discuss the problems each of these issues present as well as potential solutions.

TP.199 Multidisciplinary Planning for the Psychosocial and Legal Needs of Persons with AIDS and their Families

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Since 1985, social workers and attorneys, as members of a multidisciplinary AIDS team, have jointly addressed psychosocial-legal problems of approximately 1 out of every 3 persons with AIDS and their families followed by the team. Timely and sensitive planning for the patient's decline and death and the continued lives of family members is necessary.

Our clinical experience with a predominantly minority, both male and female, AIDS population, has identified 7 major issues affecting the nature of future planning and the options for legal intervention: 1. Relative youth of patients; 2. Existence of minor children or others financially and emotionally dependent on patients; 3. Lack of economic resources among patients and families; 4. Emotional shock and chaos following diagnosis; 5. Time limits imposed by the illness; 6. Societal bias attached to patients (due to diagnosis, ethnic or racial status, drug abuse history or sexual orientation); 7. Nature of living arrangements (unconventional but accepted patterns of extended families which confuse traditional legal responsibilities).

Early recognition of specific problems requires novel and flexible uses of such legal mechanisms as durable powers of attorney, wills and child custody and guardianship procedures. Advance legal and social planning provides security and control to patients otherwise overwhelmed by their illness. Ongoing assistance offered to families helps survivors in coping with the loss of loved ones.

TP.200 Behavioral, Immunological and Biochemical Patterns in ARC and AIDS.

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Potential markers for predicting development of AIDS were studied in 33 men with ARC. Thirty-eight healthy controls and 11 AIDS patients were also evaluated. Seven behavioral parameters (medical events, general well-being, psychological well-being, nutrition, tobacco use, alcohol use, physical activity) 6 immunological and 9 biochemical parameters were analyzed with the assistance of a computerized technique permitting pattern cognition and graphical representation of relationships among these 22 variables.

During 30 months of follow-up, 4 men with ARC developed AIDS, 15 remain healthy or have not progressed with additional ARC symptoms; 14 men were lost to follow-up. No healthy controls developed ARC or AIDS. AIDS-resistant ARC patients had a higher cholesterol (173.3), HDL (45.0), T_4/T_8 ratio (0.78) and alcohol score (80.3) compared to the pre-AIDS ARC patients (149.5), (30.0), (0.31), (70.5). Although no single variable permitted discrimination among AIDS-resistant and pre-AIDS individuals with ARC, composite computor generated patterns of multiple intersystem regulatory abnormalities at the time of initial presentation provided clear separation without overlap. We conclude that definitive early identification of pre-AIDS individuals among ARC patients is possible using routine clinical laboratory tests when combined with behavioral data.

TP.201 Predictors of chronic psychosocial disturbance arising from the threat of HIV infection: Lessons from Heterosexual, Bisexual and Homosexual Worried Well patients.

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Twenty patients presenting with high-level psychological distress in response to the threat of HIV infection were assessed on 16 psychosocial variables. All presented conspicuous management difficulties. There was a striking consistency in the presenting and background histories of patients within this group. These consistencies concerned the appearance of misinterpreted somatic features, numbers of negative antibody tests undertaken, difficulties in sexual adjustment and self-acceptance of sexuality, poor social integration, previous psychiatric/psychological history, level of physician attendance, problems of sexual expression, previous low experience of sexually transmitted diseases, obsessive-compulsive disturbances, anxiety, depression and suicidal planning.

The consistencies found in this group enable future managment requirements in this and other groups to be predicted. In addition, this analysis provides a measure of the impact of the threat of HIV in sections of low-risk heterosexual communities. It appears that 'worried well' persons with the lowest levels of objective risk frequently require a much larger amount of clinical involvement and present with a greater threat for suicidal activity than people from other groups. This is due to their higher levels of social isolation, psychological vulnerability, sexual maladjustment and guilt.

TP.202 Social Support in gay men with the Acquired Immunodeficiency Syndrome (AIDS).

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Social Support is a core requirement for human survival and it assists an individual in recovering from a major life crisis. Because most individuals diagnosed with AIDS are already partially isolated from society due to the stigma attached to homosexuality, social support networks have limited functional ability. The problem of the study sought to determine if differences exist in social support systems between gay men diagnosed with AIDS and those at high-risk for developing AIDS.

The sample consisted of 67 gay men from a metropolitan area of a conservative southern state. Thirty-six of the respondents were diagnosed with AIDS and 31 at high-risk for developing AIDS based on their sexual lifestyle. Each participant was given the Norbeck Social Support Questionnaire (NSSQ) which measures both social support networks and functional support systems.

The Mann Whitney U-Test showed no significant difference between groups in either subscale of the NSSQ. However, social network scores were far below the "norm" although functional support scores fell within normal ranges.

Social support scores from both subscales were significantly correlated with income for individuals diagnosed with AIDS and perception of health status for individuals at high-risk for developing AIDS. Neither support subscale was significantly correlated with the amount of support lost although both groups reported losses from lovers, friends, and family.

The study suggests that immediate intervention to develop and encourage social support systems is not as important as the maintenacne of support systems which are already in place.

TP.203 AIDS Education in Medical and Nursing Students: Knowledge and Attitude Correlates

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Health care provider students are often thrust into clinical environments with HIV-infected persons prior to having adequate knowledge about AIDS or HIV. In attempt to obviate this problem, a thirteen hour multidisciplinary survey elective course on AIDS-HIV was designed at UCSF and led to an enrollment of 139 medical, nursing, and pharmacy students. Prior to the first lecture, students were asked to complete an anonymous questionnaire on AIDS knowledge, attitudes, and personal demographics to determine the level of knowledge about AIDS, and to ascertain any stigmaphobias and demographic correlates which might detract from optimal clinical interactions with AIDS and ARC patients. An identical post-course questionnaire will be administered in March, 1987 to ascertain any changes.

Pre-course questionnaires indicated that 26% of medical students (MS) thought AIDS could be transmitted by mosquitoes and 18% believed AIDS could be transmitted by sweat or urine. Self identified gay/bi/lesbian (SIGBL) nursing and pharmacy students achieved slightly higher knowledge scores (97% and 88% respectively) than did their heterosexual counterparts (HC) (87% and 75%) whereas SIGBL and heterosexual MS scored equally high (88% vs. 85%). Interestingly, significantly more SIGBL medical and nursing students (60% and 100%) agreed or strongly agreed (AOSA) they had a lot of knowledge about AIDS than did their HC (16% and 28% each). 18-29% of all students AOSA that hospital employees should be allowed to refuse to care for persons with AIDS (PWA). 5-33% of all students would prefer to avoid caring for PWA. Generally, there were low rates of homophobia and ethnophobia. Post-course questionnaires will be completed in March 1987; those data will enable us to ascertain pre- and post-course correlations between demographics, knowledge, and attitudes. Verbal feedback to date indicates that AIDS education of student health care providers further decreases stigmaphobias and maximizes knowledge on AIDS and HIV. In turn, this will optimize patient care.

TP.204 The Response of Philanthropy to AIDS: A Survey of Private Giving Trends Between 1982 and 1986 to AIDS-related Issues and Implications and Considerations for Future Support

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Most philanthropy is an unimaginative, dutiful, and largely dubious process. Nearly half--$21.7 billion--of America's philanthropic contributions in 1984 went to religion; another $7.6 billion went to health care, nearly one quarter of which was used for hospital consruction--and this in a country with a surplus of hospital beds. In general, projects involving social change issues of any kind--research, conferences, publications, legal suits, large "pilot project" service organizations, and occasional grassroots groups--got less than 2.8 percent of the total. Even the Ford Foundation, considered the most adventurous of the large foundations, gave only 8 percent of its money to projects concerned with social issues. With respect to AIDS, in particular, the picture is considerably less optimistic by comparison. But the situation is changing.

Oral abstract will present a complete and current information survey on financial support for AIDS education, research, and related fields with emphasis on foundations and corporate giving programs. The survey will include the outcomes and follow-up to the five Regional Associations of Grantmakers which held meetings on AIDS in 1985. Presentation will include information on foundations and corporations which have expressed an interest in AIDS with emphasis on their giving interests: research/treatment; services; public policy, community and public education; housing and hospice programs; advocacy and civil rights for persons with AIDS. Information will also be provided about grants made-to-date, including foundation or corporation with amounts, grantee, project or purpose. Also included will be guidelines for grantmakers and grantseekers, including where support is needed plus a suggestive list of funding opportunities.

TP.205 HIV SEROPOSITIVE MOTHERS AND THEIR BABIES - DELIVERY OF HEALTH CARE.

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An epidemic of HIV began in Edinburgh amongst heterosexual intravenous drug misusers in August 1983 and had reached 50% seropositivity by 1985. Only 40% of the individuals are currently abusing and one third are female.

With the introduction of the HIV antibody test in October 1985 families with one seropositive individual and newborn babies were detected. Previous experience of this group in delivering health care had revealed default rates of 30-40%. On the 1st January, 1986 we established a separate hospital based out patient service specifically for at risk mothers and babies. This involved: 1) the joint attendance of mother, baby and/or father for health care assessment, counselling and education. 2) the service was provided by a consultant paediatrician in community health, a midwife/counsellor and a consultant in Infectious Diseases. 3) a liaison health visitor coordinates the care in the community and the referrals from 4 obstetric services. 4) where necessary the problem of non attendance has been overcome by home visiting.

To date 38 families have been enrolled in this service which consists of 3 monthly assessments. Twenty-five infants were born to 24 seropositive mothers, of whom 58% attend hospital regularly, 42% consistently utilise home visits. One family needed home visits to establish contact and encourage hospital visits. No families have been lost to follow up to date but despite intensive counselling and education 2/24 or 8% of the mothers became pregnant and required terminations.

TP.206 A Conceptual Model for a Transitional Self-Help Residence for IVDA with AIDS/ARC

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Temporary housing is needed for AIDS/ARC patients who are ambulatory and able to provide self-care but currently lack stable housing and thus, appropriate discharge and referral from inpatient settings. The NJSDH has identified an urgent need for such a resource in the Newark/Jersey City area, where most AIDS/ARC cases are related to IV drug abuse. It is hypothesized that cost-effective and humane care can best be provided in a small-scale residential facility that houses 20 persons reimbursed at a per diem rate through state funds.

To facilitate negotiations with local community groups, a conceptual model was developed. Resource development is based on the nature of the disease and the risk group to be served and is structured as part of a continuum of post-hospitalization care. Components of the model include eligibility criteria, staffing patterns and job responsibilities, daily activity schedules, rules and regulations geared toward self-care, requirements for monitoring and reporting to the funding source, and a per diem reimbursement rate lower than that for acute long-term care or residential drug treatment.

A flow chart illustrates potential patient transfers among alternative levels of care. This process is facilitated by case management.

TP.207 The Attitudes and Knowledge of Health Care Professional Working with Patients with AIDS and How They Impact on Their Professional Behavior. WILLIAM J. NELSON, W. C. HOLZEMER, M. O'ROURKE, San Francisco General Hospital, San Francisco, California U.S.A.

A survey was conducted in 3 cities of the United States. The survey was a post-test for 3 workshops on AIDS given in Anchorage, AK, Eureka, CA and So. San Francisco, CA. Sample surveyed consisted entirely of registered nurses. These nurses had worked with as few as 0-1 patients with AIDS, to 10 pts with AIDS. Academic preparation of nurses was varied. Not all nurses performed bedside care. Majority of respondants were caucasian women. A majority of nurses received their nursing education in the U.S. Purpose of the pilot study was twofold. We were piloting a new survey tool based on the works of Rubin & Peplau (1975) and Herek (1984). Main thrust of the pilot study was to look at nurses' responses to attitudinal/knowledge questions and compare those responses to questions which required a professional judgment. The null hypothesis states that essentially no differences exist between nurses in outlying areas and those closer to a major metropolitan area where AIDS was more commonplace. Early analysis of the data show: 1) nurses are open to learning about AIDS and dealing effectively with those patients, irrespective of how they may feel about homosexuality or I.V. drug use; 2) that nurses are not as homophobic as may have previously been thought; 3) that nurses work effectively with AIDS irregardless of how much exposure to AIDS the nurses have had.

TP.208 Hospital costs of patients with AIDS in Richmond, Va. L.KAPLOWITZ, J.TIPPLE, J.TURSHEN, P.MYERS, A.BERRY, L.STALOCH, Medical College of Virginia, Richmond, Virginia.

Inpatient hospital charges were analyzed for 52 AIDS patients (pts) with 98 hospitalizations(hosp) between Oct. 1983 and Dec. 1988 (range 1 to 6 hosp/pt): All were hospitalized at the Medical College of Virginia, the major facility for care of AIDS pts in central Va. Risk factors for AIDS included gay male 31, IV drug use 14, gay and IV drug 2, blood 1, heterosexual contact 4. Two were females (mean age 29.5 yrs) and 50 males (mean age 34 yrs) with 16 white, 35 black and 1 hispanic. Reasons for hosp were PCP 41, other opportunistic infections 25, bacterial infections 8, KS 2, lymphoma 1, encephalopathy 10, malnutrition or fever 9, other 2. Analysis by payor in 1986 dollars is shown:

Payors	Hosp #	Hosp Days	Avg LOS	SD LOS	Avg charge	Avg charge per diem
Blue Cross	16	212	13.3	6.8	$9631	$686
Commercial	19	337	17.7	15.5	$16027	$845
Corrections	14	245	17.5	9.1	$14991	$909
Medicaid	19	266	14.0	16.7	$9669	$735
Self pay	30	404	13.5	12.8	$10365	$1019
Total	98	1464	14.9	13.0	$11869	$860

Five hosp were over 34 days including 3 commercial (52d,50d,44d), 1 medicaid (73d), 1 self pay (62d). There is no statistical difference in charges or LOS among the payor groups. Room, lab and pharmacy comprised 68.4% of charges, ICU 7.4%, radiology, ER, OR and ancillary 14%, and diagnostic studies 10.2%. These charges are lower than initial estimates of hospital care of AIDS.

TP.209 Designated AIDS Centers/AIDS Intervention Management System (AIMS) IRA FELDMAN, R.F. HUMMEL, JUDITH SIMMONS, M.D., NYS Department of Health, Albany, NY

In January, 1986, New York State amended pertinent regulations in order to allow for the designation of acute hospitals as AIDS Centers for the care and treatment of AIDS patients. The Designated AIDS Center concept is based on a continuum of care/case management model designed to meet and/or arrange for all levels of care and needed services required by AIDS patients. This model will allow for increase access by persons with AIDS to essential health care and community resources so that AIDS patients are able to maintain the quality of their lives in a home environment as long as possible.

In conjunction with the AIDS Center process, New York State solicited competitive applications from qualified organizations for the design, implementation, and operation of an oversight system to review the performance of the comprehensive AIDS Centers, conduct a comparative review of AIDS patients, and ensure that appropriate standards of utilization review, quality assurance and case management are established and met. This oversight system is referred to as the AIDS Intervention Management System (AIMS). AIMS will centrally coordinate the retrieval of data from the multihospital treatment of AIDS patients under the case management, discreet unit model. Information concerning inpatient/outpatient services and costs as well as diagnostic and demographic data will be retrieved and analyzed in order to provide new information concerning the impact of AIDS and HIV related illness on the health care delivery system.

TP.210 Survey of United States Nursing Schools' Guidelines/Policies on AIDS CHERYL L. BOWLES, V.L. CARWEIN, Department of Nursing, University of Nevada, Las Vegas.

A descriptive survey of 242 NLN accredited schools of nursing was conducted to identify guidelines and methods used to deal with both student assignment to AIDS clients and students who are antibody positive or diagnosed with AIDS. In the absence of existing guidelines responses were based on personal thoughts or feelings.

Results indicated 95% of the schools of nursing have no guidelines for dealing with infected students, 76% have no guidelines for dealing with student assignments to AIDS clients and 49% have no plans to develop guidelines. Thirteen percent felt HIV antibody testing should be required of all nursing students and 81% disagreed.

While 66% responded that another assignment would be made if a student refused to care for an AIDS client, 45% added "other" comments, primarily student conferences and further AIDS education.

In response to dealing with antibody positive students who are not ill, 84% felt students should remain in theory and 64% in clinical. Regarding who should know the student is antibody positive, 62% felt the student health center, 35% only nursing faculty in direct contact and 51% the nursing school administration. When asked about students diagnosed with AIDS, 79% would allow theory attendance while only 31% would allow clinical attendance. Regarding who should be notified, 67% indicated the student health center, 41% only nursing faculty in direct contact and 61% the nursing school administration. Results demonstrated few schools of nursing have existing guidelines, many have no plans to develop them and uncertainty abounds in the resolution of these issues.

TP.211 HIV Infected Patients with Pulmonary Tuberculosis: Risk of Exposure for Health Care Workers (HCWs)

S.OFFUTT, ROBERT B. NADELMAN, G.P. WORMSER, NY Medical College, Valhalla, NY.

Recently, the association of TB with HIV infection has been noted. Since TB is potentially communicable to HCWs and since respiratory isolation is not routine for patients with HIV infection, we reviewed our experience with patients who had both infections. Mycobacterium tuberculosis infection was documented by culture for 35 patients at our hospital between 1/1/85 and 12/31/86. Seventeen of 18 of these patients who were tested for HIV demonstrated presence of serum antibody. Nine of these 17 patients (53%) had extra-pleural pulmonary TB (PTB) with or without other + culture sites. Six of 9 patients had sputum smears + for AFB. Respiratory isolation was instituted on admission for 4/9 (44%) of the patients, but in the other 5 (56%) PTB was not initially suspected. Time to institution of isolation ranged from 2-41 days with a mean of 8 days. Delay in instituting respiratory isolation resulted from a lower index of suspicion for TB in HIV infected patients who were initially believed to have had an alternative diagnosis. No patient had cavitary disease and only 2 had upper lobe infiltrates. Other CXR findings included 2/9 patients with only lower lobe infiltrates, 1 with only adenopathy, 1 with apical scarring, 1 pleural effusion, and 2 with a normal CXR. Six patients with PTB had a + PPD.

TB's resurgence in the HIV infected population has been characterized by extrapulmonary and non-classical infection. The frequently atypical CXR and the occurrence of skin test anergy may mask the diagnosis of PTB in the HIV infected patient. The lack of early institution of respiratory isolation in these patients may pose an increased risk of transmission of TB to HCWs. A high index of suspicion for TB in HIV infected patients will be essential in preventing nosocomial outbreaks of TB.

TP.212 Orthopaedic Surgeons' Attitudes and Practices Concerning Treatment of Patients with Human Immunodeficiency Virus (HIV) Infection PAUL ARNOW, L. POTTENGER, C. STOCKING, H. DE LEEUW, M. SIEGLER. University of Chicago, Chicago, IL.

Concern regarding a possible occupational risk of acquiring HIV infection has made some health care workers reluctant to treat AIDS patients and may influence surgeons' willingness to operate. To assess attitudes and practices of a group of surgeons that treats young and middle aged males, we conducted a questionnaire survey of all orthopaedists in the five cities with the most AIDS cases. Topics included experience, knowledge of HIV transmissibility, precautions during surgery, HIV testing of patients and surgeons, and ethical obligations of surgeons. Questionnaires were mailed during March-July 1986 and were completed anonymously by 325 of 510 orthopaedists. In the previous year, 142 (43%) had examined or operated on an HIV-infected patient, and 90% of respondents who evaluated HIV-infected patients for surgery chose to operate. Decisions to operate appeared not to be based on hospital requirements, perceived ethical obligations, or knowledge of HIV transmissibility. About half of the orthopaedists who operated considered HIV to be more transmissible than it is. Most orthopaedists felt they had the right to require preoperative HIV testing of all patients (71%) and high risk patients (85%), but such testing was ordered infrequently. Forty-three percent of orthopaedists felt patients have a right to know if their surgeon is HIV-positive, and 51% felt restrictions on the professional activities of infected surgeons were necessary. Although orthopaedists reserved broad rights for themselves, they almost always were willing to treat patients with HIV infection.

TP.213 Psychological problems in nursing patients with AIDS

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Nursing the patients with AIDS causes a lot of problems which are not comparable with those in nursing other patients with a terminal illness.Health-care personnel experiences many sources of stress leading to an emotional exhaustion.

To understand the emotional reactions and to help the staff members we performed "training cum research"groups(Balint) once a week over a half year period.

In the first months an imposing feeling of hostility against the patients with AIDS predominated.They were experienced as self-willed,demanding and conceited in a strong difference to other patients.The nurses had difficulties to assert themselves,and if they could,patients raised the feelings of not being a good nurse. Within the hospital nurses felt themself stigmatized because of nursing stigmatized patients with a stigmatized illness.The feelings and the reactions could be interpreted in the group-process as a consequence of the more or less unconscious negative attitude to the patients on one side and the identification with the mostly young,intelligent and alert homosexuals on the other side. The perception,that nearly all patients shall die let to interpretation of all their wishes as last wishes,leading to the difficulty to say "no".The more the motives of nurses became conscious,the more stress in nursing was reduced.

"Training cum research" groups seems to be a possibility to minimizestaff stress,especially the chronic professional stress syndrome.

TP.214 A Survey of Residency Programs for Persons with AIDS

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Lack of alternative housing represents a growing financial and social problem within the context the the AIDS epidemic in the US. For hospitals there is the accumulation of "Administrative Necessary Days" and for Persons with AIDS (PWAs) there is the burden of institutionalization. Various urban centers have estimated that 30% of PWAs lack appropriate alternative housing. There are several causes: patients' ostracism by family, roommates, lovers; evictions; financial straits and refusal of nursing homes and hospices to admit.

This paper is a survey of eight urban residency programs for PWAs. Half are in areas with high concentrations of PWAs. Various models are presented: small group homes, "hotels," foster homes and rent subsidies. The common thread is that while no direct health care is provided by the sponsoring organizations extensive psychosocial and spiritual support is rendered directly and health care is coordinated from hospital discharge planning through to Visiting Nurse services.

Emerging issues include IV drug abusers and neurological/physiological limitations of residents. Thus there is a need for an increase in supportive services and direct health care services. The first such programs have garnered extensive support from the Gay community and Federal demonstration grants. Future needs demand more through planning at all levels. The PWAs residency programs' home care approach provides a cost effective alternative to chronic hospitalization and an enhanced psychosocial/spiritual environment.

TP.215 Improving Utilization of Services by Families of Children with AIDS/ARC

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In 50 families with 57 children with AIDS/ARC, one or both parents are infected with HIV. Maternal risk factors were: intravenous drug use (28/50), sexual partners with AIDS or at increased risk for AIDS (16/50), maternal blood transfusion (3/5D), Haitian (2/50), and no identified risk factor (1/50). 42/57 children reside in a single parent family headed by a woman. 2/57 children were cared for by their fathers. 17/50 families were known to family protective services agencies prior to the diagnosis.

HIV infection is a family illness. 10/57 children have at least one parent who has died from AIDS. Only 3/36 parents received regular medical care. The remainder (33/36) received episodic care for acute symptoms. Illness in a parent decreased the amount of physical and emotional energy available for parenting. The combination of drug use, poverty and illness stressed an already weakened family unit.

Hospital based care services were poorly utilized. Initial home visits by a nurse and social worker lead to the development of a relationship with the family. Subsequently, 32.57 children received the following services in the home: nursing care (32/32); homemakers and home health aids (6/32); physical therapy (9/32), and speech therapy (4/32). The family with HIV infected members deals with multiple stresses on a daily basis. Assuring continuity between hospital and home while providing care in the home can result in improved utilization of services in both settings.

TP.216 Treatment of AIDS-related Kaposi's Sarcoma (KS/AIDS) by Alpha-2-recombinant Interferon and Bleomycin.

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The efficacy of recombinant leukocyte A interferon (Roferon) treatment of KS/AIDS has been previously evaluated. We have showed response of KS/AIDS to bleomycin alone (Second Intern. Conf. on AIDS. Paris 1986). In a pilot study, we evaluated Roferon in combination with bleomycin. Roferon was given I.M. at 18 Mu daily for one month and was continued at the same dose three times weekly. A slow continuous infusion of bleomycin was given I.V. at 6 mg/m^2 daily for 3 days each month. Treatment was continued unless tumor progressed.

In october 1986, the first 9 patients were enrolled in this prospective study. All patients were homosexual men with disseminated KS. No patient had received treatment for KS. Preliminary results indicate that 2 had a complete response, 3 a partial response, 3 a stable disease. One patient developed Pneumocystis carinii pneumonia. Final results will be presented on all the patients treated for more than 3 months.

TP.217 INHALED PENTAMIDINE AS EXCLUSIVE THERAPY FOR PNEUMOCYSTIS CARINII PNEUMONIA (PCP) IN THE ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS).

J.A. Golden, H.Hollander, J.E.Conte,Jr. University of California,San Francisco, CA. The treatment of PCP is associated with side-effects in over 50% of AIDS pts. We therefore assessed the efficacy of inhaled pentamidine (P) in AIDS pts with mild PCP (defined as PO_2>60mm Hg). Pts inhaled P (4 mg/kg) daily for 14 days by nebulization ("Ultra Vent," Mallinckrodt, St.Louis). P levels by HPLC were assessed in bronchoalveolar lavage (BAL) and plasma. Nine pts were entered into they study. Six pts favorably responded to inhaled therapy with resolution of dyspnea, fever, and improved chest x-ray and arterial blood gases. One pt failed after 5 days of inhaled P; two pts became ineligible for the study after less than 48 hrs when they clinically deteriorated and were no longer considered mild PCP. There were no serious adverse effects of inhaled P although 2 pts had P-related cough. Inhaled P resulted in P base concentrations (see table) in BAL that were higher and plasma levels significantly lower than levels in our pts treated with intravenous P (BAL P level 7.15±5.3 ng/ml; plasma level 286±171 ng/ml) consistent with the efficacy of inhaled P and lack of adverse effects in this study. Inhaled P should be further investigated.

Pt #	P[1] Concentration in BAL (ng/ml)	Day[3]	Plasma (ng/ml)[4]
1	ND[2]	-	3.1
2	55.3±17.1	1	14.7
3	28.6±10	4	16.9
4	66.8±16	3	0
5	16.8±7.3	1	2.5
6	30.6±27.5	14	32.8

1. Mean ± SD; 2. Not done; 3. day(s) of therapy prior to BAL; 4. peak concentration measured post inhalation, day 1

TP.218 Use of Imuthiol (Diethyldithiocarbamate, DTC) in Symptomatic HIV Infection.

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To determine whether Imuthiol improves clinical and immunologic status, we studied the drug in symptomatic AIDS and ARC patients (pts). 44 pts were stratified and randomized to receive either 200 mg/m^2 IV weekly for 4 months or no therapy, followed by crossover to the opposite arm for an equal period. Both groups have been followed with the same clinical and immunologic parameters, and all pts had evidence of severe immune deficiency at entry. No significant toxicity has been observed. Analyses of results from the first 4 months prior to crossover indicate that treated pts show a trend towards reduced progression (p=.231) and are significantly more likely to show improvement in symptoms (p=.002) and reduction in lymphadenopathy (p=.005) than untreated pts. One treated pt each showed disappearance of marked splenomegaly, hairy leukoplakia, and intractable perianal monilia. One pt with Kaposi's sarcoma confined to lymph nodes showed partial histologic remission. No significant changes in lymphocyte surface markers, lymphocyte blastogenesis, or skin test reactivity were seen.

These results indicate a possible role for immunorestorative therapy in symptomatic HIV infection. Double-blinded, placebo-controlled studies are under way to confirm and extend these findings.

TP.219 Use of High Dose Oral Ketoconazole in AIDS patients for Prevention of Relapse in Cryptococcal Meningitis. TIMOTHY P. MESS, WK Hadley CB Wofsy. San Francisco General Hospital, San Francisco, U.S.A.

From April 1985 to December 1986, 35 patients with cryptococcal meningitis (CM) were seen at SF General Hospital. 22/35 patients (63%) completed 6-8 weeks of induction treatment with Amphotericin B with or without 5-FC. 13 died during induction. Because recurrence is high (30-60%), an open study with high dose (1000mg) oral ketoconazole (KCZ) was begun in June 1985 for patients who had completed an induction treatment with Amphotericin B. 20/22 patients who completed induction were offered KCZ prophylaxis, a demented patient and a non-compliant patient were excluded. 15/20 eligible patients chose KCZ.

Of the 15 patients who received KCZ, 7 are still alive without evidence of relapse, range 4-11 months post diagnosis of AIDS and CM. 6 patients have died with a range of survival post diagnosis of CM of 6-11 months (median 7.5) and a range of survival post diagnosis of AIDS of 8-14 months (median 8.5). One of these patients relapsed after 5 months of KCZ therapy and died 2 months later due to active CM. One had an excellent clinical response during 4 months of KCZ and died 1 month after discontinuing KCZ. The other 4 deaths were unrelated to CM. One lost to follow-up was still free of CM after 7 months of KCZ. 2 patients stopped KCZ secondary to toxicity. One stopped KCZ after 2 weeks due to a >10-fold increase in LFT's and died 2 months later. The other stopped KCZ after 3 months due to abdominal pain and died 5 months later without evidence of relapse. 3/13 remaining patients had mild nausea. MIC's to KCZ were available on 13 patients with a median value of 1.56ug/ml (range 0/39-3.13). 12 serum KCZ levels on 8 patients were available with a median value of 3.79ug/ml (range 2.24-15.0). CSF KCZ levels on 2 patients failed to detect KCZ. Only 1/12 (8.8%) patients had evidence of CM relapse while on KCZ. Whether KCZ is as effective or as toxic as weekly Amphotericin remains to be studied.

TP.220 D-penicillamine(DPA) Treatment for Lymphadenopathy Syndrome (LAS) and AIDS-Related Complex (ARC)

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DPA has been shown to inhibit HIV replication in vitro. We assessed the clinical, virologic and immunologic effects of 3 different daily oral regimens of DPA in 24 HIV-infected homosexual men who had: (1) HIV isolated from peripheral blood mononuclear cells (PBMC), (2) T4/T8 < 1.0, (3) absolute T4 100-500/mm^3, and (4) depressed lymphoproliferative responses (LPRs). 19 patients had LAS, 5 had ARC. 10 PTS received oral high dose (HD) DPA (2 gm) for 2-6 wks. 7 were treated with low dose (LD) DPA (0.5 gm) for 12-18 wks. 7 PTS are receiving intermediate, intermittent dose (ID) DPA (1 gm), alternating 4 weeks on drug with 4 weeks off. One PT each in the HD and LD groups stopped therapy because of a drug induced skin rash. Therapy was discontinued in 8 HD, 2 LD and 2 ID PTS because of a decrease in T4 or LPR of $\geq$ 50%. HIV expression was assessed by measuring reverse transcriptase activity and by detection of p17 and p24 antigens in PHA-activated PBMC co-cultured with H9 cells. HIV expression in LD PTS was unchanged whereas all HD PTS had reduced HIV expression. Complete inhibition was seen in 3/5 HD PTS who received DPA for 6 weeks, without re-expression for at least 6 weeks after stopping therapy. Two patients treated for at least 4 weeks had detectable serum p24 antigen before treatment which decreased by 20% and 60% respectively with treatment. Reversible depression ($\geq$ 20%) of T4 counts was seen in 5/10 HD, 4/7 LD, and 4/7 ID PTS; depressed LPR ($\geq$ 40%) in 7/10 HD, 2/7 LD, and 2/7 ID PTS. DPA has promising in-vivo anti-HIV activity, but further study is needed in order to define a regimen which both inhibits HIV replication without depressing T-cell numbers or function.

TP.221 *Fansidar prophylaxis of Pneumocystis carinii pneumonia in asymptomatic HIV + persons and persons with ARC.*

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Pneumocystis carinii pneumonia is the most common initial, life-threatening opportunistic infection in persons with AIDS. Mortality from the first episode of PCP is as high as 20-30%. Safe and effective prophylaxis would be worthwhile to prevent the morbidity and mortality associated with PCP.

30 patients with T4 cell counts 250 were randomized to receive Fansidar (1 tablet weekly) or placebo. Patient groups were comparable in terms of age, T4 counts, baseline hematology and chemistries. All were followed every three weeks.

There were 4 episodes of PCP during the mean follow-up period of 7 months, all occurring in the placebo group. One of these was fatal. In the placebo group lab studies were stable except for increases in LDH and decreases in Hgb and leukocyte counts in patients developing PCP. In the Fansidar recipients mild toxicities included nausea (4/15) and rash (1/15) not requiring discontinuation of drug. Progressive anemia (2/15) and severe leukopenia (3/15) required dosage modification or discontinuation of the drug in 1 patient.

In summary, Fansidar may provide effective prophylaxis for first episode PCP. Bone marrow suppression may be a significant limitation to prolonged use in some patients. The use of folinic acid supplementation may help reduce this drug-induced morbidity.

TP.222 Phase I Tolerance Study of HPA-23 in Patients with AIDS and Preliminary Data of Anti-HIV Activity

HPA-23 COOPERATIVE STUDY GROUP. (BRUCE L. MOSKOVITZ, Rhone-Poulenc, Inc., Monmouth Junction, N.J.)

The heteropolyanion HPA-23 is active against HIV in vitro and was selected for study as a potentially effective antiviral compound for patients with AIDS. Sixteen, 16, 23 and 14 patients with AIDS received, respectively, 0.25, 0.5, 1.0 or 2.0 mg/kg daily doses of HPA-23, intravenously-administered, five days weekly (Monday-Friday) for up to eight weeks to assess the tolerance of HPA-23. Clinical changes and anti-HIV activity were monitored periodically.

Forty-three of the 69 patients completed the entire eight-week course. Thirteen discontinued because of a concurrent illness, six discontinued because of a clinical adverse event, and seven discontinued because of laboratory test abnormalities (thrombocytopenia-6, 4+ proteinuria-1).

HPA-23 produced a dose-dependent decrease in platelet count and increase in SGOT values. Other adverse events included leukopenia, granulocytopenia, fever, diarrhea and nausea.

Over the eight-week course of treatment, no improvement in immunological function, measured by total lymphocyte count, T_4 cell count, and T_4/T_8 ratio, was observed.

No changes in clinical symptoms, development of new opportunistic infections, or occurrence of Kaposi's sarcoma lesions were apparent.

Qualitative results of reverse transcriptase activity assays suggested a dose-dependent anti-HIV effect.

We conclude that the toxicity of HPA-23 is predictable and acceptable. Longer-term studies to assess drug concentration-effect relationships, in vivo antiviral activity, and clinical efficacy of HPA-23 are warranted.

TP.223 Open Study of AL-721 in HIV-Infected Subjects with Generalized Lymphadenopathy Syndrome (LAS).

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Eight subjects with LAS associated with HIV infection consented to an open 8-week trial to evaluate the antiviral and immunologic effects of AL-721. CD4/CD8 ratios were less than 0.7 and CD4 counts below 550 cmm. The drug was administered in 10 gm frozen sachets and reconstituted twice daily in 10 ml chilled orange juice before a fat-free breakfast and after a low fat dinner. Surveillance studies were conducted of clinical state, serum lipids, lymphocyte subsets, lymphoproliferative responses, and reverse transcriptase assay (RTA) following cocultivation of peripheral blood mononuclear cells.

There were no significant drug-related clinical events during the 8 weeks of drug and the 8 weeks follow-up period. Seven patients remained clinically stable throughout the study and follow-up period. One patient, however, who always had less than 35 CD4+ cells, developed disseminated CMV after 4 weeks off drug and cerebral toxoplasmosis after 10 weeks off drug. Serial RTA were performed in 7 with detectable RT at baseline having an initial mean level of 73,419 cpm decreasing to a mean 44,653 at 6 weeks and 27,419 at 8 weeks. These changes in mean values resulted from decreasing levels in 5 of the 7 subjects. Pokeweed mitogen responses increased in 5 of 8 so that the baseline mean of 18,000 cpm rose to 30,300 at 4 weeks and at 28,923 at 8 weeks and then subsequently decreased to 18,223 at 4 weeks following treatment. No significant effects on serum lipids or T lymphocyte subsets were noted.

The results of this study suggest that AL-721 may exert an anti-HIV effect and augment immune responses in subjects with LAS.

TP.224 Combination Chemotherapy and Interferon in Kaposi's Sarcoma (KS) and AIDS. F.A. SHEPHERD, M.B. Garvey, W.K. Evans, M.M. Fanning, M. Kline, and S.E. Read. University of Toronto, Toronto, Canada.

Thirteen males, median age 37 years (range 28-46), with extensive KS and AIDS were treated with combination chemotherapy and Interferon. There were four patients with stage III and 9 with stage IV disease (one pulmonary and 8 G.I. involvement). Treatment consisted of monthly courses of actinomycin-D, 1 mg/m^2 and vinblastine, 6 mg/m^2, day 1; bleomycin, 10 mg/m^2, day 1 and 8; and human lymphoblastoid Interferon, 10 million units/m^2 i.m. 3 times per week x 6 doses starting day 14. Forty-one treatment cycles were administered (median 3, range 1-12). Complete response was seen in one patient (24 weeks), and partial response in 4 patients (14-44 weeks). One patient had mixed response with regression of extensive skin involvement, but progression of pulmonary disease. Median survival of the group was 48 weeks (4-143+ weeks). Eleven patients died of progressive KS, one with lymphoma, and one with Pneumocystis pneumonia. Nausea and vomiting was mild to moderate and easily controlled. All patients had slight temperature elevation and muscle aches while receiving Interferon, both easily controlled with antipyretics. The median granulocyte and platelet nadirs at day 14 prior to starting Interferon were 600 x 10^9/L and 134,000 x 10^9/L, respectively and did not fall further while on Interferon. Four patients required hospital admission for neutropenia associated fever. Comparison of pre- and post-treatment T-cell subsets, 2'5'A synthetase levels, and mitogen responses demonstrated no improvement while on Interferon.

Although a significant number of patients achieved response with this combined modality therapy, we feel that the duration of response, survival, and toxicity suggest that this form of therapy is not appropriate for patients with KS associated with AIDS.

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TP.225 Effect of AZT Therapy on Quantitative Serum HIV Antigen.

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To determine the effect of AZT therapy on quantitative serum HIV antigen (Ag), we serially studied 18 HIV culture positive AIDS patients treated with AZT in accordance with the BW-AZT protocol. HIV Ag was determined prior to therapy and weekly thereafter using a commerically available enzyme immunoassay (Abbott Laboratories) which detects the p24 gag gene product. T-cell subset analysis was determined monthly. Ten of 18 patients were HIV Ag positive prior to the initiation of therapy. There was no significant difference in mean T-helper cell counts (67 vs 109/mm^3) or T-suppressor cell counts (412 vs 1012/mm^3) between HIV Ag positive and negative patients, respectively. In 9 HIV Ag positive patients with a mean pre-therapy quantitative Ag of 253 pg/ml (range: 23-804), the Ag decreased by a mean of 223 pg/ml (92% reduction) with a range of 56-731 pg/ml (range: 56-100% reduction) after one week of AZT (1200 mg/day). In one patient HIV antigen decreased by 1961 pg/ml (80% reduction) after 4 weeks of AZT (1200 mg/day). Dose reduction of AZT (600 mg/day) in 2 patients was followed by slight increases in HIV Ag. AZT had to be discontinued in 7 patients after 12-46 days (intercurrent opportunistic infection, 3; toxicity, 3; progressive deterioration, 1). HIV Ag increased by a mean of 721 pg/ml (range: 30-2927) within a mean of 6.6 d (range: 2 to 11) of discontinuing AZT. Four of 8 patients who were HIV Ag negative at initiation of therapy became transiently HIV Ag positive within 3 weeks of beginning AZT. Initiation of AZT therapy in HIV Ag positive patients with AIDS is followed by a rapid decline in HIV Ag which rapidly returns to pre-therapy levels after AZT is stopped. This suggests that serial quantitation of HIV Ag may be a useful parameter by which to monitor AZT therapy. The clinical significance of this is as yet undetermined.

TP.226 Preliminary Data From a Phase I Study of Oral Ribavirin (RIB) in Children with AIDS-related Complex (ARC).

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We are presently conducting a Phase I study to determine safety, tolerance, and pharmacokinetics of single and multiple doses of oral RIB (1-beta-D-ribofuranosyl-1,2,4-triazole-3-carboxamide) is stable children with ARC. This is an open study with sequential dose escalation. Patients were excluded if they had severe or progressive end organ disease. Five patients were enrolled in the first group (3 female, 2 male); mean age 26.2mo (16-61mo). Six mg/kg RIB was dissolved in 3ml water and given po after 6-8hr fast. Safety parameters included: vital signs, physical exam, stool guiac, CXR, EKG, C8C, platelet ct., reticulocyte ct., SMA-18, urinalysis, PT/PTT. Patients readily took the drug and all tolerated it well. All parameters remained stable except HGB which decreased, mean 0.78gm (0.1-1.5gm). This was greatest for the smallest children, could be accounted for by blood drawing and was associated with appropriate increase in reticulocyte ct. One patient developed mild eosinophilia. Following a single 6mg/kg dose mean peak plasma RIB concentration was 2.5uM (1.02-3.96uM) and occurred 1-2hr post dose. During multiple dosing the range of trough conc. at steady state was 2.05-2.8uM at 30 days and 1.85-2.9uM at 60 days.

During the two months of this study parents reported decreased night sweats, increased activity and improved appetite. In addition, lymphocyte phenotyping was performed at baseline and after 30 and 60 days of daily RIB administration. There was a general trend toward increase of absolute number and percentage of T-helper cells with improvement in helper:suppressor cell ratios. We are now proceeding with dose escalation.

TP.227 A phase II Study of Beta$_{ser}$ Interferon Given Subcutaneously to Patients With AIDS Related Kaposi's Sarcoma.

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Beta$_{ser}$ Interferon has shown antiproliferative activity in several neoplasms and has in vitro antiviral activity against the human immunodeficiency virus (HIV). To date we have treated 15 patients with AIDS related Kaposi's Sarcoma subcutaneously with 90 x 10^6 IU qd x 5 each wk. for 12 wks. Two patients had prior pneumocystis carinii pneumonia. Five had received prior chemotherapy, and 12 had positive culture for HIV prior to starting treatment and are evaluable for antiviral activity. Fourteen patients were stage II and one was stage IV. Of 15 evaluable patients, 3 had partial responses, 5 have stable disease and 6 had progressive disease. One patient had an opportunistic infection (M. Tuberculosis) diagnosed while on study. To date, 2 of 4 patients who have had sequential HIV cultures have become culture negative. Toxicity has been mild with no grade 2 toxicity seen in any patients. Side effects have been limited to fever, chills, malaise and local skin reactions at the site of injection. Preliminary results of T-cell subsets are presented below.

	Time on Study (months)			
	1 (n=13)	2 (n=10)	3 (n=4)	4 (n=2)
Leu 3 pre Rx	1048±628	1151±680	991±274	957±378
post Rx	747±500	905±611	1208±830	1301±535
Leu 2 pre Rx	220±203	273±201	384±187	236±69
post Rx	156±150	148±167	348±173	202±44

Beta$_{ser}$ Interferon appears to be a well tolerated treatment with in vivo activity against AIDS related Kaposi's Sarcoma.

TP.228 Clinical and Immunological Response to IMREG with ARC/AIDS Patients. S, LANDESMAN*, ADRIEN MARCEL*, M. MURALI*, H. DREW*, M. GOTTLIEB**, A. GOTTLIEB**. SUNY Health Science Center at Brooklyn*. Brooklyn, N.Y., IMREG Inc.**, New Orleans, La.

Sixteen patients with HIV disease (12 with AIDS related complex (ARC) and 4 with AIDS) received 6 biweekly intradermal injection of IMREG-I in a phase II clinical trial. IMREG-I is an immune modulator comprised of a small molecular weight peptide prepared by a series of dialysis and HPLC separations from human leukocytes. At entry the average T_4 cell numbers for ARC and AIDS subjects were 309(62-761) and 51(0-71) respectively. Seven ARC and four AIDS subjects were anergic to PPD, tetanus toxoid and candida. Three ARC patients had minimal skin test reactivity (<5mm induration) to tetanus toxoid alone.

Nine of the 10 anergic ARC and 2 AIDS subjects regained full skin test reactivity to tetanus toxoid (8-30mm induration).

While there was no change in absolute numbers of T_4 cells in these subjects, the response to 1.0 ug/ml of PHA (studied sequentially in 9 subjects) increased 2 to 4 fold in 7 patients and was unaltered in two.

Associated with therapy was the resolution of constitutional symptoms such as fever and night sweats in 9 patients. There was no loss of body weight in any patient. The hematocrit and platelet counts were stable. No toxicity was noted with use of IMREG-I. These data suggest that IMREG-I has some reconstitutive effect on the cell mediated immune response in these patients as judged by skin test reactivity and pHA responsiveness. No conclusion as to the long term efficacy of IMREG-I can be made based on this limited trial. Further studies are in progress.

TP.229 LONG TERM FOLLOW-UP OF 82PATIENTS TREATED BY RECOMBINANT ALFA 2 INTERFERON IN AIDS RELATED KAPOSI'S SARCOMA.

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Over a 4 years period, 82 male patients (homosexual or bisexual) with a mean age of 38.7 years (range : 24-55) with AIDS-related Kaposi's Sarcoma (KS) were treated (83 courses) with recombinant leucocyte interferon alfa 2A (r IFN alfa 2A). Two types of dosage regimen were used : 36 million unites (n=16) and 18 mu (n=67).

43 patients had cutaneous and/or lymph node KS, 30 had cutaneous and/or mucosal KS, 10 cutaneous and/or visceral KS. 24 patients (29%) had a complete response (CR) with a mean duration of 10.6 months (range :1-36 months). 6 of them relapsed within 12.5 months (r : 4-28 months) after discontinuation of treatment, 2 responded completely with a new course of IFN. 9 patients had a partial response, 5 of them relapsed. None of the patients died in these groups.

The CR rate was higher in the group of patients who had only cutaneous and/or lymph node KS (37%) in comparison with the group who also had mucosal (23%) or visceral lesions (10%).

None of the patients with prior or concomitant opportunistic infection had a CR, neither did patients who had a positive CMV blood culture. Other factors which seem to be of relevance for the responding groups are: lymphocyte count, absolute number of auxillary (CD4) cells, CD4/CD8 ratio, response to recall antigens, serum B2-microglobuline level, serum IgA. r IFN alfa 2A is efficient in controlling AIDS-related KS, its effect on life expectancy should be evaluated.

TP.230 Treatment with high doses of immunoglobulins in HIV-related thrombocytopenia.

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In our Clinic a severe idiopathyc thrombocytopenia (<15.000 PLT x mm^3) was observed during the early phases of HIV infection in 21 out of 451 patients affected with LAS. These patients were in the most part asymptomatic. We treated with human immunoglobulins (0.4 g/kg daily for 5 days - Venoglobulines Mérieux) 10 thrombocytopenic patients (7 males, 3 females; age 20 to 27) presenting with hemorrhagic symptoms (3 purpuras, 3 metrorrhagias, 2 epistaxis and 2 hematomas due to microtraumas). A rise of platelets count was recorded since the third day of treatment; by the fifth day nine patients were showing a four-fold increase of their platelets (PLT x mm^3 55000 ± 9000). Platelets, however, returned to initial values 3 to 4 weeks after therapy was discontinued. In all but one patient (a woman with metrorrhagia) clinical symptoms subsided. In conclusion, i.v. infusion of immunoglobulins at high doses in HIV-positive patients with thrombocytopenia seems to represent a rather effective therapeutic approach; in our view, however, it should be considered in symptomatic patients only.

TP.231 Pharmacokinetics of Oral Azidothymidine (AZT) in 5 AIDS Patients.
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Limited pharmacokinetic data are available on AZT. We studied 5 AIDS patients (4 male, 1 female; age range 19-32 years) receiving AZT after recovery from an initial bout of Pneumocystis carinii pneumonia. 200 mg AZT was administered PO every 4 h. Patients had sera drawn for pharmacokinetic analysis on the first dose according to the following sampling scheme: pre-treatment, 10, 20, 30, 45, 60, 90, 120, 180, 240 mins. Fifty sera were analyzed for AZT by HPLC. AZT serum conc. (Cp)-time data were subjected to model independent pharmacokinetic analysis. Mean pharmacokinetic parameters (n = 4) were: AUC, 4.09 ± 1.29 μM hr; T 1/2, 0.6 ± 0.25 hr; TBC/F, 3260 ± 896 ml/min. The average Cp max was 3.54 μM, which occurred 0.75 - 1.5 h post AZT dose. Cp min at 4 h. was < 0.5 μM in 4/5 patients. One patient was treated separately. His AUC (10.18 μM hr) and TBC/F (1230 ml/min) were substantially different (by a factor of >2) than the other 4 patients. This could not be explained on the basis of renal or hepatic dysfunction and may be a result of concurrent drug therapy affecting AZT metabolism. Further investigations are in progress. The previously estimated minimum level for in vitro antiviral effect with AZT is 1 μM. In our 5 AIDS patients receiving 200 mg PO q 4 h, AZT Cp were only above 1 μM for 1-1 1/2 h out of each 4 h dosing interval. This may not be sufficient to control viral replication in all patients and, if dosage is reduced due to toxicity we predict Cp will almost always be below 1 μM.

TP.232 **The Efficacy of Azidothymidine in the Treatment of Patients with AIDS and AIDS-related complex: a double-blind placebo-controlled trial.**
THE AZT COLLABORATIVE WORKING GROUP.

To determine the efficacy of Azidothymidine, AZT, a double-blind placebo-controlled trial of oral AZT was conducted in 282 patients with AIDS and AIDS-related complex at 12 medical centers. Patients were preatratified according to CD4 cell numbers and randomly assigned to receive a capsule containing either 250 mg of AZT or placebo every 4 hours for a total of 24 weeks. The study trial was terminated prematurely in September, 1986. One-hundred forty-five patients received AZT, and 137 patients received placebo. Twenty-seven patients had completed 24 weeks of the study; the remainder had completed at least 8 weeks. Nineteen placebo recipients and 1 AZT recipient died during the study (p<0.001). This increased likelihood of survival was comparable for patients with AIDS and AIDS-related complex who received AZT. Forty-five patients receiving placebo developed opportunistic infections compared to 24 receiving AZT (p<0.001). Six AZT recipients and 10 placebo recipients developed Kaposi's sarcoma (p>0.20). A statistically significant increase in the number of CD4 cells was noted in patients receiving AZT compared to those receiving placebo (p<0.001). After 12 weeks, the number of CD4 cells among AZT recipients with AIDS returned to pretreatment values. Similar trends in CD4 cell numbers were also noted among AZT recipients with AIDS-related complex but were less prominent. Twenty-nine percent of patients receiving AZT developed cutaneous hypersensitivity reactions compared with 9% receiving placebo (p<0.001). AZT appeared to prolong and improve the quality of life in a select group of patients with AIDS and AIDS-related complex over a 24 week period.

TP.233 Anti-HIV Seroconversion in Haemophiliacs Receiving Heat-Treated Concentrates.
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In the UK, about two thirds of factor VIII used is imported commercially from the USA. The remainder, and all factor IX, is derived from domestic (NHS) volunteer plasma. In December 1984, when heated concentrates were first introduced, 78% of patients attending the RFH Haemophilia Centre who had been exposed to US commercial factor VIII in the preceding six years were anti-HIV seropositive. All 52 patients who had only received NHS concentrates were seronegative. At that time at least, therefore, HIV contamination appeared much less likely in domestic products. 82 patients seronegative at the time of their first exposure to heated products have been followed to December 1986. Of the 30 who received factor IX concentrate, all remain seronegative (total 35 exposure years). Of the 52 who received VIII concentrate (31 'wet heated' commercial, 18 'dry heated' NHS, 3 'dry heated' commercial) 49 remain seronegative (64 exposure years). 2 patients receiving 'wet heated' commercial VIII seroconverted within 4 months of starting treatment with heated product. However, both had received incriminated lots of unheated NHS VIII before changing to heated factor VIII. A third patient, treated with 'dry heated' commercial VIII derived from non-anti-HIV screened donors, seroconverted 8-10 months after starting heated product. Although this patient had also previously received an incriminated lot of unheated NHS concentrate, HIV transmission by the 'dry heated' commercial concentrates seems more likely.

TP.234 The Infectivity of Anti-HIV Positive Blood Components
STEVEN KLEINMAN*, THE TRANSFUSION SAFETY STUDY GROUP**, *American Red Cross, Los Angeles, CA, **other participating institutions.

To determine transmissibility of HIV by transfusion, the Transfusion Safety Study retrospectively tested donor sera collected in late 1984 and early 1985 in five areas with high AIDS prevalence. The rate of anti-HIV positivity among 91 recipients of blood components from anti-HIV(+) donors (by EIA, IB, and RIP) was 89% 12-18 month post-transfusion. The 10 anti-HIV(-) recipients did not differ from the anti-HIV(+) by age or underlying disease. By blood component type, positivity rates were 91% (51/56) for RBC, 100% (10/10) for platelets, 83% (5/6) for WB, 100% (2/2) for leukocyte poor blood, 85% (11/13) for FFP, and 100% (2/2) for cryoprecipitate. One anti-HIV(-) recipient and one anti-HIV(+) recipient received components from the same donation. Two of two recipients of washed RBC were anti-HIV(-); recipients of previous donations by the same donors were anti-HIV(+), indicating the potential infectivity of these donors. A third anti-HIV(-) recipient received only a few ml of RBC. Two other anti-HIV(-) recipients received components (FFP and RBC) from the same donor, suggesting that this donor was not infectious. These findings have important implications for assessing the importance of anti-HIV screening, the risks to recipients of components from anti-HIV(+) donors, and for establishing lookback policies.
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TP.235 Improved Anti-HIV Screening Assay Using Recombinant Antigen Based Conjugate
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Two major antigenic proteins of HIV, ENV and CORE, have been cloned and expressed in E. coli by recombinant DNA (rDNA) methodology and purified by immunoaffinity chromatography. These purified antigens were coated onto polystyrene beads which are used to capture anti-HIV from the specimen. Anti-HIV bound to the beads was detected in the assay using a probe solution containing rDNA HIV antigens coupled to horseradish peroxidase (HRPO). Unlike currently licensed anti-HIV tests, this assay requires no sample dilution and is capable of detecting IgG, IgM and IgA. This recombinant antigen based screening assay is 8 to 64 fold more sensitive than current anti-HIV tests and shows significantly improved specificity. When 125 sera reactive by the current anti-HIV test but negative by Western Blot were tested, all were negative in this assay. 68 AIDS sera and 250 sera testing positive by current EIA and Western Blot were reactive in this assay.

Serial bleed studies indicate that the rDNA based screening assay can detect anti-HIV seroconversions significantly sooner than current tests. As configured, this assay does not allow differentiation between anti-CORE and anti-ENV reactivity. rDNA CORE and ENV may be separately coated onto beads and coupled to HRPO to make tests which will discriminate anti-CORE and anti-ENV positivity.

TP.236 Prognostic Importance of Western Blot HIV Antibody Patterns in HIV Antibody Positive Hemophiliacs
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Antibodies to specific HIV viral antigens were measured by a Western blot system using biotin-avidin detection (Biotech Research Labs, Rockville MD) on 36 HIV antibody positive hemophiliacs (HTLV-III ELISA, DuPont) on whom serial samples were available between 1977 and 1986, representing 2 to 8 years following seroconversion. Of these, 20 were Class IV (9 AIDS, 7 ARC, 4 other) and 16 were asymptomatic. At seroconversion, antibody to p24 (gag) appeared first, followed by antibody to gp41 (env); antibody to p55 (gag) was weak or absent at seroconversion in 26, developing one to three years after seroconversion in six of 26 or not at all in three of 26. Thirteen of 20 Class IV (8/9 AIDS, 2/7 ARC, 3/4 other) hemophiliacs lost (or never developed) antibody to one or more HIV gag (p15, 24, 55) or pol (p31, 53, 64) antigens, as compared with one of 16 asymptomatic hemophiliacs ($X^2 = 12.81$, $p < .001$). The development of AIDS was preceded (one to four years) by the loss/lack of antibody to p15 (in 5 AIDS patients), p53 (in 4), p24 (in 3), p55 (in 3), p64 (in 3), and p31 (in 2), each $p < .05$ as compared with non-AIDS patients. Absence of antibody to more than one (2-5) HIV antigens occurred in five of eight AIDS patients. The single AIDS patient with no loss/lack of antibody was the only one with lymphoma and no opportunistic infection. In conclusion, the loss or lack of antibodies to gag (p15, 24, 55) or pol (p31, 53, 64) HIV gene products appears to be associated with and occurs within one to four years before the development of AIDS in HIV antibody positive hemophiliacs.

TP.237 Frequency of Recent Blood Donation in HIV Infected Soldiers
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In October 1985, the Department of Defense mandated screening all active duty soldiers for the presence of antibody to human immunodeficiency virus (HIV). Data assessing frequency of recent blood donation by HIV infected soldiers and rate of infection in product recipients has important disease control implications.

One hundred seventy-four HIV infected soldiers from a broad geographic distribution were ascertained through general (not blood bank) screening. Each soldier was evaluated for a history of blood donation between March 1983 and April 1985. Twenty-six percent (45/174) reported donating at least once during that period; a rate almost ten times higher during this interval than reported for persons subsequently diagnosed with ARC and AIDS. A centralized effort to "look back" at living recipients of components donated by HIV-Ab positive soldiers ascertained through blood bank screening is in operation. Seven living recipients have been evaluated; 5 (71%) are HIV-Ab positive by western blot. Two recipients were infected as long as 22 months before determination of positivity in an asymptomatic donor. Although 70% of HIV infections in the Army are determined by methods other than blood donor screening, "look back" does not currently include prior donations from soldiers determined HIV-Ab positive by other than blood bank screening.

These data describe a situation with far-reaching disease control consequences. Increased effort to evaluate and improve donor self-deferral and "look back" is essential.

TP.238 HIV Infection in the Edinburgh Haemophiliac Cohort
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We previously reported on a cohort of 33 haemophiliacs who were transfused in April 1984 with a single batch of factor VIII contaminated with HIV. In our initial study we found that 15 patients had developed anti-HIV antibodies, but we have since identified 3 later seroconverters. We now report a 4 year follow up of this cohort.

Patients who became seropositive received significantly more bottles of the contaminated batch of factor VIII. All patients receiving more than 30 bottles became seropositive. The annual factor VIII consumption was significantly greater in the seropositive group. Thirteen patients developed HIV-specific antibodies within 15 weeks of exposure to the contaminated batch, whereas 4 patients developed antibodies more than 20 weeks after exposure, and one patient between 11 and 36 weeks after exposure. There were no differences in total dose of batch received, annual factor VIII consumption, pre-exposure T4/T8 ratios or absolute T4 counts between early and late seroconverters. Mean T4 counts in the seropositive group have declined from 0.73 x 10^9/l before exposure to 0.33 x 10^9/l at the time of writing. Mean T4 counts in the seronegative group have remained static at 0.77 x 10^9/l. In the seropositive group one patient has AIDS, 3 have ARC, 3 have PGL and one has thrombocytopenia. Ten seropositive and all the seronegative patients remain asymptomatic.

TP.239 Transfusion-Associated Transmission of Human Immunodeficiency virus (HIV) from a Seronegative Donor - Coloraoo
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In November 1985, a male donor at a Colorado blood collection facility was seropositive for HIV antibody (ELISA and Western Blot) although previously donated units (August and April 1985) were ELISA negative. Recipients of the April 1985 donation were seronegative by ELISA when tested in May 1986.

The 2 recipients of the August donation were subsequently found to be seropositive. Recipient #1, who had no other risk factors for HIV infection, received units from 15 different donors. Recipient #2, who had other risk factors for HIV infection, received units from 3 different donors. Another donor (seronegative April 1986) was common to both August recipients. Of the remaining 14 donors, 12 resided in Colorado and were seronegative when retested 5 months or more after the August donations. Two donors outside Colorado have not been tested.

Interviews of the seropositive donor and recipients suggest donor infection through sexual contact 12 weeks or less prior to his August donation when he may have been falsely negative on ELISA or viremic but without detectable antibody. Sexual contacts (18) of the seropositive donor and 2 recipients were identified. Of those in Colorado (11), all were located, 9 tested and 2 seropositive. Contacts outaide Colorado (7) have not been notified.

This is the first reported case of HIV transmission from a seronegative blood donor since screening for HIV antibody in blood collection facilities.

TP.240 Confidential Exclusion of Donated Blood: Evidence for Donor Compliance.
J. PINDYCK, B. HOSEIN, A. WALDMAN, W. YING, M. LOWY, and C. BIANCO, The New York Blood Center, New York, N.Y. 10021.

Recognition that AIDS was a disease transmissible by blood necessitated introduction of stringent measures to ensure safety of the blood supply. Early in 1983, The New York Blood Center introduced a questionnaire which allows individuals who appear medically acceptable as blood donors to review, before their donation, information about high risk of exposure to AIDS. They are then asked confidentially to designate their donations "for transfusion" or for "laboratory studies only". This system has been maintained in addition to the ELISA assays for antibodies to HIV, introduced in April of 1985, because the population of self-excluders may contain individuals who are exposed to HIV, but have not yet developed detectable antibodies.

Analysis of results from 459,165 blood donations show that the 98.2% who designated their units "for transfusion" had HIV antibody prevalence of 0.09%, while the 1.8% who designated their units "for studies only" had a prevalence of 2.1%. The prevalence of Hepatitis B surface antigen was 9 times higher among "for studies" donors than among "for transfusion" donors. These differences were highly significant ($p<0.001$) indicating that many donors are aware of their higher risk of exposure to HIV, find it difficult not to donate at a blood drive, and therefore designate their units "for studies only", in compliance with systems designed to improve the safety of the blood supply.

TP.241 MECHANISM OF B CELL DYSFUNCTION IN HAEMOPHILIA
RAJAN MADHOK, JAGRACIE GDO LOWE CD FORBES
UNIVERSITY DEPT. OF MEDICINE GLASGOW ROYAL INF .SCOTLAND

In a previous study we showed a significant increase in serum IgG levels in HIV positive haemophiliacs (INT.CONG.AIDS PARIS 1986) we have investigated the mechanism of this increase in both HIV positive (asymptomatic) and HIV negative haemophiliacs.

In all positive patients the increase was polyclonal. Using the T cell dependant B cell mitogen PWM our results show significantly higher levels of spontaneous IgG secretion in both positive and negative patients relative to normals. No further increase on PWM stimulation was seen. Using the T independent B cell mitogen Staph.Aureus Cowan strain I, no significant change was seen in positive patients. The T 4 cnt in HIV positive pts. showed corre.coief. of .57 with spontaneous IgG secretion.

	HIV POS		HIV NEG		CONTROL	
	UNSTIM	STIM	UNSTIM	STIM	UNSTIM	STIM
PWM	320	290	115	128	97	110
STAPH	320	370	115	115	97	80

medians are shown Non parametric stats.

The B cell dysfnc. in HIV positive haemophiliacs appears to be both due to T4 cell depletion and a intrinsic B cell defects.

TP.242 Detection of Human T-Cell Lymphotropic Virus-I (HTLV-I) Antibodies by an Enzyme Immunoassay (EIA).
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An EIA has been developed to screen blood components for antibodies to HTLV-I, the virus linked with Adult T-Cell Leukemia (ATL) and implicated in other diseases as well. The format of the HTLV-I test is identical to that of the Du Pont HTLV-III antibody screening test, allowing the two tests to be used simultaneously. Simultaneous testing for HTLV-I and III antibodies may become necessary if the risk of contracting HTLV-I infection from contaminated blood products is eventually judged unacceptably high. Simultaneous screening may also become common clinically if the prevalence of dual infection with HTLV-I and III increases, either through HTLV-III infection of previously HTLV-I infected individuals or through spread of HTLV-I by the same risk factors as for HTLV-III. Preclinical evaluation of the HTLV-I EIA confirms that it is both sensitive and specific. 24 of 24 ATL patients were reactive, while only 4 of 1,752 (0.2%) individuals at low risk for HTLV-I infection were reactive. HTLV-III antibodies are not reactive in the HTLV-I EIA. Sera from a group of intravenous drug abusers were screened with the HTLV-I and III EIAs and western blot (WB) tests. 10 individuals reactive on the HTLV-III WB were nonreactive on the HTLV-I EIA but reactive on the HTLV-III EIA. 9 individuals reactive on the HTLV-I WB are reactive on the HTLV-I EIA but nonreactive on the HTLV-III EIA. Another 10 individuals reactive on both HTLV-I and III WB were reactive on both the HTLV-I and III EIAs. The HTLV-I EIA and a confirmatory WB test are currently being clinically evaluated at several blood research centers in the United States.

TP.243 SCREENING OF VOLUNTARY BLOOD DONATIONS FOR ANTIBODIES TO HUMAN IMMUNODEFICIENCY VIRUS (anti-HIV) - EIGHTEEN MONTHS EXPERIENCE
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By November 1986 the Canadian Red Cross had screened 1.25 million blood donations for anti-HIV using the Abbott enzyme immunoassay (EIA). Blood found repeatedly reactive by EIA is discarded and the antibody status is confirmed by Western blot (WB). The data indicate that during the first six months of testing, initially EIA reactive, repeatedly EIA reactive and WB positive rates gradually decreased. During the subsequent seven months, however, there was a gradual increase in all three rates. It is not clear whether this is due to modifications in the test system or to changes in the donor population. Data was also analyzed in terms of geographic location, sex, age and frequency of donation. Prevalence of anti-HIV in urban donors was approximately four times greater in rural donors. Although the highest incidence of AIDS is reported in the Province of British Columbia, the highest anti-HIV prevalence was observed in the Province of Quebec. The highest anti-HIV prevalence was in male donors between 30-39 years of age. Nationally, the WB rate fluctuated from a high of 0.034% in November 1985, to a low of 0.008% in May 1986. The data indicate that in spite of the inherent problems with the WB system it is still very important in establishing the donor antibody status. Data which will have been accumulated on the screening of over 1.82 million donations by the end of April 1987 will be analyzed for presentation of additional information.

TP.244 HIV-seropositive hemophilia cohort in follow-up since 1983: Virologic, immunologic and clinical relationships.
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Since longitudinal studies are needed to establish the effect of HIV infection on the immune system, we have chosen to follow-up a cohort of patients with coagulation defects (>245 subjects). While 41.5% of 79 HIV-seropositive hemophiliacs have a LAS and 11.4% (9 patients) a lesser AIDS, 5.1% (4 patients) have come down in 1986 with AIDS (3 AIDS/OOI, 1 AIOS/KS). Comparison of case/control matched HIV-seropositive, symptomatic subjects with seronegative, asymptomatic ones revealed a significant reduction of T-helper to T-suppressor ratio ($p<0.001$) and absolute T-helper cell counts ($p<0.001$) as well as an increase of T-suppressor cells ($p<0.01$) in the seropositive group. Furthermore, a significant increase of urinary neopterin levels was observed in that group. Analysis of the antibody profile to herpesviruses showed elevated anti-EBV-VCA titers (IgG) with a 4-fold increase of geometric means in case/control matched seropositive subjects. Moreover, they have significantly more ($p<0.005$) IgM antibodies to EBV-VCA. There was no association however with antibodies to CMV, HSV-1 and HSV-2. These findings strenghten the concept that LAS may be the result of an important interaction between EBV and HIV in hemophiliacs, since both viruses may be responsable for polyclonal B-cell activation.
Furthermore, data will be presented on correlations between neutralizing antibodies to HIV, antibody detection by IIF and Western blot analysis compared to immunological profiles and clinical evolution of this AIDS risk group.

TP.245 UV-Laser Inactivation of Virus in Blood Products.
KRISTINA N. PRODOUZ*, J.C. FRATANTONI*, N.A. LOWEN*, P. ALBRECHT* and R.F. BONNER**, FDA* and NIH**, Bethesda, MD.
Evaluation of UV radiation to selectively inactivate virus in blood products was conducted by uniform treatment of attenuated poliovirus, platelets and plasma with 40 nsec pulses of 308 nm (UVB) radiation emitted by a XeCl excimer laser. Dose rates and doses of UVB were varied from 0.1 to 1.3 MW/cm^2 per pulse and 0.51 to 53.7 J/cm^2, respectively. Virus and platelet samples were prepared in isotonic phosphate buffer containing 5% albumin. Biologic activities measured included: 1) cytopathic effect of the virus; 2) platelet aggregating activity; 3) spontaneous release of serotonin from platelets; and 4) plasma prothrombin time (PT) and partial thromboplastin time (PTT). Poliovirus showed a dose-dependent titer decrease of 4 to 6 $\log_{10}$ with UVB=10.8 to 21.5 J/cm^2. Although rate and amplitude of platelet aggregation decreased in a dose-dependent manner over the range of UVB doses used, at UVB=10.8 to 21.5 J/cm^2 aggregation amplitude was decreased 20-30%. At UVB=10.8 J/cm^2 serotonin release was 5% above control, while at the highest dose of UVB (53.7 J/cm^2), 10% was released from irradiated platelets. Plasma proteins were minimally affected by UVB=10.8 J/cm^2: PT 10% above control, PTT 7.5% above control. With UVB=21.5 J/cm^2, PT and PTT of irradiated plasma were <20% above control. The observed inactivation of a hardy virus by doses of UVB which do not abolish the biological activity of platelets or plasma proteins suggests that UV-laser treatment is a potential method for diminishing the viral bioburden of blood products containing anucleate cells.

TP.246 FOLLOW-UP OF WESTERN BLOT POSITIVE BLOOD DONORS-VICTORIA,AUSTRALIA.
*K.McGrath, **A.Mijch, **W.Maskell, **T.Howard, *J.Morris, **C.R.Lucas et al. (**Fairfield Hospital, Melbourne Australia. *Victorian Blood Transfusion Service, Victoria Australia.)
Nationwide blood donor screening was introduced in Australia on 1st May 1985. In Victoria sera repeatedly reactive by Enzyme Immuno Assay (EIA) (Electro Nucleonics Inc.) were referred to the State Reference Laboratory for confirmatory testing by Western Blot (WB). Sera were regarded as positive if precipitin bands were detected at p24 and/or at p41 as recommended by C.D.C.[] Of 214,699 donors screened in the first 12 months 924 (0.4%) were repeatedly reactive by EIA; 15 of these(0.0065%) were positive by WB (p24 in 5, p41 in 2, p21 plus p41 in 7). [] Fourteen were referred for clinical assessment (10F & 4M). Their ages ranged from 21 to 49 years. No donor admitted to risk factors for HIV infection; 10 were married (8F & 2M) and one divorced (F). All were asymptomatic. One donor had generalised lymphadenopathy and physical examination was normal in the others. [] Among spouses, tests for anti-HIV by EIA were negative in all 10 and by WB in the 7 tested. [] Of 27 cultures for HIV from 14 donors only one, from the donor with lymphadenopathy, was positive. [] The 14 WB positive donors have been reviewed on 3 to 8 occasions over 4 to 17 months. Each has remained well and lymphadenopathy has not been detected in the follow-up examinations of the donor in whom it had been initially present. [] In subsequent serological testing 5 have become negative by EIA and 13 of 14 remain positive by WB (p24 in 7, p41 in 2, p24 plus p41 in 4).
Our experience suggests that in this population the majority of donors reactive by WB test are not infected with HIV. This has resulted in modification of both WB interpretation criteria and blood donor notification policy in Victoria.

TP.247 Risk Factors for Antibody to HIV in New York Blood Donors: Validation of AIDS Risk Classification and of Confidential Donor Self-Exclusion at the Time of Donation
CHARLES S. RABKIN*, N. VAN DEVANTER**, W. E. EWING***, and J. PINDYCK**, *CDC, Atlanta GA, **NY Blood Center, ***NYC Dept. of Health, New York NY.
We studied blood donors in the New York metropolitan area, a region of high incidence of AIDS, to determine prevalence of antibody to HIV, risk factors for seropositivity, and potential sexual transmission. From April 1985 - May 1986, the Greater New York Blood Program collected 470,000 blood units, 8000 of which were confidentially donor-designated to be used for laboratory studies only. Anti-HIV by Western Blot was present in 337 (0.08%) units donated for transfusion and in 133 (1.6%) units donated for studies (relative risk = 20). Two hundred-fourteen seropositive donors from both groups have been interviewed, 169 men and 45 women. One hundred twenty-nine (90%) of 144 donors for transfusion and all 70 donors for studies had known risk factors for AIDS: male homo- or bisexuality (62%), intravenous (IV) drug use (4%), male homo- or bisexuality and IV drug use (6%), blood transfusion (1.4%), and sexual contact to a member of an AIDS risk group (15%). Fifteen seropositive donors, 12 men and 3 women, had no known AIDS risk factors. None of the 15 had received hepatitis B vaccine, acupuncture, or artificial insemination, and none was a health care worker; 2 had received immune globulin since 1978, and 5 reported prostitute contact 1 to 5 years before interview. Twenty-two sex partners of seropositive blood donors of opposite sex were also studied; anti-HIV was detected in 2 of 3 bisexuals, in 1 of 2 IV drug users, and in 1 transfusion recipient, but not in 16 heterosexual partners without other risk. Despite a high endemic incidence of AIDS in the New York area, anti-HIV is rare in blood donors, most seropositives are in known AIDS risk groups, and new risk factors are not apparent in seropositives not in risk groups.

TP.248 Analysis of discrepant anti-HIV ELISA reactives. D. THOMAS, F.K. MUNDON, D. ZIMMERMAN, D. LARSON, L. GOWAN, and S. WILHELM, Electro-Nucleonics, Columbia, MD 21046.
Conflicting results are sometimes obtained in tests for the presence of antibody to HIV in plasma and serum samples, depending on the particular kit being used in the screening test. We examined samples from thirty-three blood bank donors with histories of repeatedly reactive plasma. Of 33 samples received, 19 were reported to be repeat positive when analyzed in a competitor's test at the blood bank. Comparative testing with reagents from two other manufacturers showed that inconsistencies were present within the ELISA data generated from the different kits. We have used 3 independent methods (Western blot, IFA, and competition with labelled anti-HIV human antiserum) to further analyze these plasma samples. For seven of the eight samples which demonstrated Western blot reactivity, the results indicated the presence of antibody only to a protein with M_r = 24,000. The eighth sample (sample 5) contained antibody to other HIV proteins in addition to p24. Only 2 of the 33 samples appeared positive by IFA. These IFA results were confirmed independently by an outside laboratory. The IFA-negative samples could not compete with authentic anti-HIV human antisera for binding to plates that contained bound HIV protein. In this same competition assay, however, sample 5 showed complete inhibition of binding; sample 14 showed partial inhibition. We conclude that the use of Western blot as a confirmatory test may be misleading in the case of "p24 only" reactivity, and all but 2 of the 19 samples originally designated as repeat reactives must be considered to be false positives.

TP.249 AIDS STUDIES IN KENYAN HAEMOPHILIACS

Dr. G.W. Kitonyi, M.R.C.Path., Prof. T. Boury, M.R.C.Path
Prof. E.G. Kaalli, M.D., M.R.C.Path., University of Nairobi, Kenya.

Fifty one consecutive black Kenyan patients with haemophilia A (40), Christmas disease (8) and Von Willebrand's disease (3) were tested for HTLV-III antibodies with an ELISA test. Positive results were confirmed by Western blot analysis. 12 of the 40 patients (30%) with haemophilia A were seropositive. None of the patients with Christmas disease or Von Willebrand's disease were seropositive. Our results indicate a link between the use of commercial factor VIII concentrates and seropositivity.

These studies also indicate that the rate of exposure of the Kenyan haemophiliacs to the HLV-III virus is not as high as reported elsewhere. This is probably related to limited use of factor concentrates in Kenya due to the prohibitive cost of the concentrates. None of the 51 patients has clinical AIDS but 4 seropositive patients have extrainguinal lymphadenopathy.

Although there are many studies on sexually transmitted AIDS in black Africa, there are very few reports on AIDS studies on haemophiliacs. This paper represents one of the few reports on AIDS studies in black African haemophiliacs.

Ongoing work includes T-cell subset studies and attempts to isolate the AIDS virus from the patient.

TP.250 HIV Infection: Surveillance of Heat Treated Factor VIII in the UK Criteria Based on Retrospective Studies of Unheated Factor

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Criteria are given for defining a transmission event of HIV from heat treated factor VIII and IX concentrates to man. Retrospective information was obtained appertaining to the use of seven batches of unheated factor VIII and one batch of factor IX concentrate in patients from England. Seven out of 22 (32%) patients seroconverted with the batch of factor VIII for which most information was available. The attack rate of HIV antibody negative haemophiliacs receiving this batch was seven out of 12 (58%). There were 13 seroconversions amongst the 179 (7.3%) haemophiliacs who had received factor VIII concentrates from one of seven batches. One patient seroconverted of 24 (4%) who had received factor IX concentrate from one batch for which there was information. Three individuals had HIV antibody before exposure to this batch so the TRUE ATTACK RATE was 1 in 17 (6%). The batches of unheated concentrate were used between 1981 and 1985. Testing of recipients started in the autumn of 1984. The total number of seroconversions was 14 out of 203 patients (7%) and the attack rate corrected for known prior exposure in 36 individuals was 14/167 (8%). A strategy for the surveillance of heat treated factor is proposed.

WEDNESDAY, JUNE 3

Plenary Session IV

W.1.1 Public Health Measures for Prevention and Control of AIDS
DONALD R. HOPKINS, M.D., Centers for Disease Control, Atlanta, Georgia, USA

Epidemiological surveillance, epidemiological research, and laboratory research are the basis for existing and potential interventions to help prevent and control the unprecedented threat posed by AIDS and HIV infection. Dissemination of information to the public, health education, individual counseling and testing of persons whose actions or circumstances put them at increased risk of infection, prevention and treatment of I.V. drug abuse, and serological screening of donated blood, sperm and organs are the main public health measures which are now available. The extent of application of these measures varies widely in different target U.S. populations. All require thorough evaluation. Asymptomatic infectious persons are the largest source of new infections; they need to know that they are infected, and be counseled as quickly as possible. Even partly successful drugs to delay onset of symptoms in infected persons would provide a significant new incentive for potentially infected persons to be tested voluntarily, but the scope of this pandemic will be decided before any vaccine or curative therapy is available for general use, if ever. Strong informed leadership is required at all levels to minimize irrelevant distractions and keep attention focused on the most important issues in this life and death struggle.

W.1.2

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

W.1.3 Significant Contributions of Community Organizations

PAULA VAN NESS, Former Chair of National AIDS Network; Centers for Disease Control, Atlanta, GA, USA.

The AIDS crisis has presented multiple challenges to communities throughout the world. In the United States a network of community-based organizations, now spanning all 50 states, has developed over the past few years. In the absence of a vaccine and effective treatment for the infection, these community-based organizations have borne the brunt of developing and maintaining cost-effective social service programs and educational efforts to reduce transmission of the virus and to counter unwarranted fear in the general public. Working in conjunction with other public and private organizations on the community and national level, these organizations have also contributed significant leadership in identifying community needs and promoting other groups' involvement in providing information/education and vital human services to their constituencies. Specific examples of the significant accomplishments of these organizations will be discussed and analyzed.

W.1.4 Research on HIV infection among intravenous drug users: State of the art and state of the epidemic.

Don C. Des Jarlais, New York State Division of Subtance Abuse Services, New York, N.Y.

As the largest group of heterosexuals infected with HIV in the United States and Europe, intravenous drug users will play a key role in the future of the AIDS epidemic in those regions. This presentation will review emerging critical issues in HIV infection among IV drug users. In epidemiology there is not yet a satisfactory explanation of the great geographic variation in seroprevalence rates nor a good understanding of the efficiency of heterosexual transmission to non-IV drug users. In natural history, HIV infection appears to lead to a variety of fatal outcomes in addition to surveillance definition AIDS; co-factors for infection outcomes need more intensive study. In prevention, basic AIDS education does lead to risk reduction, but methods of increasing risk reduction have not yet been fully assessed.

Epidemiology—Heterosexual Transmission

W.2.1 Multicenter Study of HIV Antibody in U.S. Prostitutes
W.W. DARROW, J.B. COHEN, J. FRENCH, P. GILL, R.K. SIKES, J. WITTE, et al., CDC Collaborating Group on HIV in Selected Women, Atlanta, GA, USA.

To assess seroprevalence of antibody to human immunodeficiency virus (HIV) and risk factors for a positive anti-HIV test, we are studying women who have engaged in prostitution since 1978. Prostitution is defined as the exchange of oral, vaginal or anal sexual exposures for money or drugs. Serum is tested for HIV antibody by an enzyme immunoassay supported by Western blot assay, for hepatitis B seromarkers by radioimmunoassay, and for antibody to syphilis by RPR and MHA-TP, confirmed by FTA-ABS. As of January 28, 1987:

	Number positive/Number tested (percent)		
Research Site	Anti-HIV	Hepatitis B	Syphilis
Las Vegas	0/26 (0)	4/20 (20.0)	0/18 (0)
Colorado Springs	1/67 (1.5)	12/54 (22.2)	0/52 (0)
Atlanta	1/92 (1.1)	26/82 (31.7)	11/87 (12.6)
Los Angeles	7/136 (5.2)	78/109 (71.6)	38/119 (31.9)
San Francisco	7/126 (5.6)	41/102 (40.2)	9/102 (8.8)
Miami	40/210 (19.1)	93/169 (55.0)	81/179 (45.3)
Newark-Jersey City-Paterson	9/13 (69.2)	12/12 (100.0)	2/13 (15.4)

Women with antibody to HIV tended to have seromarkers for hepatitis B (odds ratio=4.6; CI=2.3-9.2) and antibody for syphilis (OR=2.1; CI=1.2-3.8). Measures of parenteral drug use, especially "shooting gallery" attendance (OR=4.0; CI=2.1-7.5), and unprotected sexual exposures with many "nonpaying" partners (r=.124) were associated with a positive anti-HIV test, even after effects of place were statistically controlled. About 80% reported using condoms, but only 8 women had used them with each vaginal exposure. All 8 were anti-HIV negative. Treatment for drug addiction and the proper, more frequent use of condoms should reduce risks of HIV infection in female prostitutes.

W.2.2 Human Immunodeficiency virus (HIV) among Female Prostitutes in South Florida.
MARGARET A. FISCHL, GM DICKINSON, S FLANAGAN, MA FLETCHER. University of Miami, Miami, Florida.

To evaluate the prevalence of HIV infection among sexually active heterosexuals, prostitutes in south Florida were evaluated. Prostitutes from an ecooomically depressed inner city area and a middle class urban area were recruited. Ninety prostitutes from an inner city area were studied. All were between 17 and 28 years of age, from the lower socioecooomic group, had less than 12 years of education, and had arrest records. Sixty used intravenous drugs. Thirty-seven (41%) had anti-HIV antibody. Of the 63 who used intravenous drugs, 29 (46%) had antibody to HIV, and 8 (30%) of the 27 who did not use intravenous drugs had antibody to HIV. Factors associated with HIV antibody ($p<0.05$) included a greater number of clients per week (28.7 $\pm$ 5.2, seropositive group; 20 $\pm$ 11.7 seronegative group), number of black clients (49% vs. 15%), participation in vaginal intercourse (60% vs. 26%), hepatitis B antibody (58% vs 23%), syphilis (68% vs. 30%), number of pregnancies (3.8 $\pm$ 2.0 vs. 1.8 $\pm$ 1.3), and gynecologic surgery (87% vs. 37%); whereas, a negative assocation ($p>0.05$) occurred with length of prostitution, out of town clients, repeat clients, working outside the south Florida area, and fellatio.

Twenty-five women from escort services were also studied. All were between 21 and 32 years of age, from the middle socioeconomic group, and were high school graduates. None had anti-HIV antibody.

These data suggest that inner city prostitutes in south Florida have a high prevalence of HIV antibody and that the major risk factors for infection appear to be both intravenous drug use and multiple heterosexual partners from an area with a high incidence of AIDS.

W.2.3 AIDS and HIV Infection, Belle Glade, Florida.
KENNETH G. CASTRO*, S.LIEB**, C. CALISHER*, J.WITTE**, H.W. JAFFE*, THE FIELD STUDY GROUP, *Centers for Disease Control, Atlanta, GA, & Fort Collins, CO, **Florida Department of Health & Rehabilitative Services, Tallahassee, FL, USA

We studied the occurrence of AIDS and HIV infection in Belle Glade, Florida, because of the high cumulative incidence rate of AIDS (375/100,000) and high proportion (8/62; 13%) of AIDS patients with no identified risks. Most of the AIDS patients resided in an area characterized by high rates of intravenous (IV) drug abuse and sexually transmitted diseases. Nineteen (32%) of 59 adults with AIDS could be directly linked to at least one other reported AIDS case by sexual contact, sharing of needles during IV drug abuse, or both. From February through September 1986, we conducted a community-based seroepidemiologic study to identify risk factors for HIV infection. Twenty-nine (3%) of 844 adults tested had antibody to HIV, including 17 (4%) of 441 men and 12 (3%) of 403 women. The highest age-specific rate (6%) was among persons aged 18-29; no person over age 60 was seropositive. None of 144 children aged 2-10 years had antibody to HIV. No clustering of infected persons within households occurred, except for infection in sex partners. Compared with adults who were seronegative for HIV antibody, adults with HIV antibody were more likely to have antibodies to hepatitis B virus (56% vs. 25%, p<0.001) and to Treponema pallidum (58% vs. 22%, OR= 5.0, p<0.001). The presence of antibodies to five arboviruses prevalent in south Florida or the Caribbean was not significantly correlated with HIV infection. In Belle Glade, the high cumulative rate of AIDS appears to be the result of HIV infection in IV drug abusers and their sexual partners; transmission through mosquito vectors is unlikely.

W.2.4 Case control study of HIV-seropositive versus HIV-seronegative European expatriates in Africa
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Of 3805 European expatriates screened at the Medical Center, Ministry of Foreign Affairs, Brussels or the Hospital for Tropical Diseases, in Antwerp, 27 (0.7 %) were HIV-antibody positive in 1985, and of 4398 European expatriates tested in 1980, 46 (1 %) were HIV seropositive, including the 27 of 1985 (38 M and 8 F). A standardised questionaire was offered to 30 seropositives (24 M and 6 F) between June and December 1986, asking for residence, sex-life and other risk-factors. 49 (39 M and 10 F) sero-negative European expatriates were recruited as controls at teh same centers in November and December 1986, and matched for age, sex and residence. European male seropositive expatriates had significantly more sex-partners ($p < 0.0001$), more contact with prostitutes ($p < 0.001$), and more injections ($p < 0.05$) by less qualified personnel ($p < 0.01$) than seronegative controls. There was no significance in dental interventions, use of condoms, ano-rectal sex, and a history of STD. There were no active homosexuals, IVD addicts or blood-recipients amongst this group. There were no significant differences between the 6 female seropositives and their controls, exception made for having seropositive (promiscuous) partners. It is concluded that HIV infection in European expatriates in Africa is mainly heterosexually acquired, and that prostitute contact is a major risk factor.

W.2.5 Heterosexual Transmission of Infection and Disease by the Human Immunodeficiency Virus (HIV).
NEAL H STEIGBIGEL*, D.W. MAUDE*, C.J. FEINER*, C.A. HARRIS*, B.R. SALTZMAN*, R.S. KLEIN* et al.,*Montefiore Med. Ctr., *A. Einstein Coll of Med., Bronx, NY.; CDC, Atlanta, GA; NIH, Bethesda, MD; USA.

We report on a longitudinal prospective study, initiated in July, 1982, of the potential for the heterosexual transmission of HIV infection and disease. Thus far, 100 steady heterosexual partners (HP) (88 females, 12 males) (with no other AIDS risk factors) of 97 pts. with AIDS or ARC have had detailed st'dized interviews, physical exams, immunologic studies and tests for HIV antibody by EIA, confirmed with Western blot. Screening was repeated every 4-6 mos. HP were followed for a median of 10 mos. (range 1-44). Median number of estimated sexual encounters was 152 (range 8-945) (during period from 18 mos. prior to symptom onset in pt. to last sex).

48 of 100 HP (48%) had antibodies to HIV: 41 of 88 females (47%) and 7 of 12 males (58%). Of sero(+) HP, 20 (42%) had clinical or lab. AIDS-related abnormalities: 2 had AIDS (1 died), another died with persistent generalized lymphadenopathy (LA) and dissem. tbc., 14 had LA with low T-4 cells (one had oral candidiasis and one H. zoster), 3 had either LA or low T-4 cells.

There were no significant assoc's. between serologic status and duration of relationship, number of episodes of sexual contact, sex during menses or serologic markers for CMV or hepatitis B.

Anal intercourse was significantly assoc. with seropositivity (p=.02). Female sero(+)'s were recipients of analingus ($p<.01$) and oral semen ejaculate ($p<.01$) more often than sero(-) women. However, none of these activities were required for seropositivity. Sero(-) HP used barrier contraceptives significantly more often then those who were sero(+) ($p<.05$), but 49% of HP who did not use them remained sero(-).

This study indicates that both male and female steady HP of pts. with AIDS or ARC are at substantial risk for HIV infection and related disease.

W.2.6 Heterosexual Transmission of Human Immunodeficiency Virus (HIV): Association with Severe T4-Cell Depletion in Male Hemophiliacs.
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Since 1984 this cohort study has evaluated risk factors for HIV infection in the female sexual partners of HIV+ men with hemophilia. Of the 38 known female partners, 24 (63%) participated in the 1986 follow-up. Of 14 non-participants, 1 had AIDS 2 years after her husband, 1 was tested HIV+ after her husband had AIDS, 5 were clinically well, and 7 could not be contacted. HIV antibody prevalence in participating women increased from 0/10 in October 1984 to 4/24 (17%) by September 1986. Three of the 4 HIV+ participating women had documented HIV seroconversion more than 4 years after their male partner's seroconversion, and the fourth was sexually exposed to an HIV+ hemophiliac for only 5 months. The dominant risk factor for HIV infection appeared to be the male partner's most recent T4 count (Table, trend p=.01):

	T4 cells/ul in male	HIV in female
HIV infection was not inevitable, in that 5/5 women were HIV- after more than 5 years of sex with an HIV+ hemophiliac. All 4 HIV+ women had vaginal intercourse without a condom, but risk of HIV did not appear to be affected by frequency of sex or by hysterectomy. Other sexually transmitted diseases, anal intercourse, or sex during menstrual periods were not necessary for HIV infection.	0-99	3/6
	100-349	1/7
	350-549	0/6
	>550	0/5

Thus, HIV transmission can occur after years of routine vaginal intercourse especially once the male has severe immune deficiency. These findings suggest that rapid replication of HIV and death of T4 cells may be linked in vivo, with low T4 counts heralding a high risk of both AIDS and sexual infectivity. If true, effective antiviral drugs may reduce not only AIDS but also incident HIV infections.

Virology—Vaccines

W.3.1 Expression of HIV Genes by Recombinant Vaccinia Viruses
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Recombinant vaccinia viruses that express HIV env, gag, pol and tat genes were made. When the entire open-reading-frame for the env gene was expressed, gp160 was synthesized, cleaved to form gp120 and gp41, and transported to the cell surface. Both gp160 and gp41 were exclusively cell associated whereas approximately half of the gp120 was in the medium. Exclusive synthesis of gp120 was obtained by introducing a stop codon before the cleavage site. The majority of gp120 made under these conditions was extracellular and the electrophoretic mobility of the protein was similar to that of the cleaved product of gp160 indicating that the transmembrane and anchor sequences were not necessary for glycosylation or transport. Enhanced expression of the entire gp160 gene and the truncated gp120 form were obtained with a newly developed hybrid vaccinia virus/bacteriophage T7 expression system. The entire gag-pol region was expressed by recombinant vaccinia virus, as an immunoreactive protein of approximately 55,000 daltons. Neither frame-shifting nor proteolytic processing occurred to a detectable extent. Active reverse transcriptase was made by a recombinant vaccinia virus that contained a pol gene engineered to contain a translation initiation codon at its start. Tat expression was achieved by still another recombinant vaccinia virus.

These recombinant vaccinia viruses are being used to produce neutralizing antibody, determine cytotoxic T cell targets, investigate proteolytic processing and transport, study receptor binding, and analyze inhibitors of enzyme activity.

W.3.2 A Neutralizing Monoclonal Antibody Reactive against an External Envelope Glycoprotein of HTLV-III/LAV (Human Immunodeficiency Virus)
SHUZO MATSUSHITA*, A.KOITO*, H.SUTOH*, T.HATTORI*, M.ROBERT-GUROFF**, K.TAKATSUKI*, *Second Division of Internal Medicine, Kumamoto University Medical School, Kumamoto 860, Japan. **Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda Maryland, USA.

We report the production and characterization of a monoclonal antibody reactive against an external envelope glycoprotein (gp120) of human T-lymphotropic virus type III(HTLV-III/LAV). Gp120 has been associated with virus infectivity and cytopathology including cell fusion. We immunized mice with glycoprotein fraction of viral antigens (HTLV-IIIB isolate) and obtained a clone (designated as 54'C), which was secreting monoclonal IgG1 antibody reactive against 120 kilodalton(kd) molecule of the purified virion in a Western blotting assay. This antibody (designated as 0.5B) bound to the surface of HTLV-III infected H9/IIIB cells but not to uninfected H9 cells. 0.5B immunoprecipitated 160 kd and 120 kd molecules from extracts of endogenously radiolabelled H9/IIIB cells. 0.5B crossprecipitated gp160 and gp120 recognized by antibodies in the serum from patients with AIDS. Gp160 and gp120 have been identified as virus encoded envelope gene products of HTLV-IIIB. Neutralizing activity of the antibody was evaluated by infecting the susceptible T-cell line with cell free virion. 0.5B inhibited the infection of HTLV-IIIB in a dose dependent manner as detected by immunofluorescence assay. We also tested the antibody with syncytia induction inhibition assay using virus producing H9/IIIB cells. Inhibition of syncytia formation was observed in the presence of 0.5B antibody. These results suggest that 0.5B antibody reacts with an external envelope protein of HTLV-III. 0.5B antibody may have diagnostic or therapeutic value.

W.3.3 Extensive heterogeneity of HIV genomes in vivo.
MICHAEL SAAG*, J. GIBBONS*, W. PARKS**, E. PARKS**, F. WONG-STAAL***, R.C. GALLO***, G. SHAW*, and B. HAHN*. *University of Alabama at Birmingham, Birmingham, AL, **University of Miami, Miami, FL, and ***Laboratory of Tumor Cell Biology, NCI, Bethesda, MD.

The AIDS virus, HIV, has been shown to exhibit striking genomic variation when isolates obtained from different individuals are compared. To assess the extent of genetic variation present in vivo we isolated HIV from peripheral blood mononuclear cells of two infected patients (RJS and MPF), generated large recombinant lambda phage libraries, and identified and characterized multiple clones of HIV to search for evidence of genomic diversity in vivo. Thirty full-length viral clones from the RJS library and 16 full-length viral clones from the MPF library were obtained and analyzed via restriction endonuclease mapping using Sst I, Eco RI, Bgl II, Hind III, Pvu II, and Pst I. Out of 30 RJS clones, 13 highly related yet genetically distinct genotypes were evident. Of the 16 MPF clones, 9 highly related yet distinguishable genotypes were apparent. Certain genotypes were represented by more than one clone and these, in turn, were evident as predominant species on the original Southern blot patterns of infected cellular DNA. HIV passaged in vitro by sequential limiting dilutions requiring multiple rounds of replication did not exhibit similar degrees of genomic variation. These data indicate that (i) extensive genetic variation is generated in vivo; (ii) the degree of viral heterogeneity has heretofore been underestimated; (iii) many different viral forms coexit in persistently infected individuals, and thus, "isolates" obtained from such persons for use in the study of HIV biology and immunology, unless cloned, are actually complex mixtures of genetically-distinct viruses.

W.3.4 Full-length and truncated HIV Envelope Polypeptides Produced in an Insect Cell Expression System Elicit High Titer Neutralizing Antibodies in Animals.
Gale Smith*, M.A. Cochran*, B.L. Ericson*, M. O'Shaughnessy**, T. Folks***, M. Martin***, et al., *MicroGeneSys, West Haven, CT, **Laboratory Centre for Disease Control, Ottawa, Canada, *** NIAID, Bethesda, MD.

Recent efforts to develop subunit vaccines against the human acquired immune deficiency syndrome (AIDS) have focused on the HIV envelope proteins. Sera from individuals infected with the HIV virus often contain high titer antibodies directed against the viral envelope; however, these antibodies are not protective and usually exhibit low-level neutralizing activity *in vitro*. This apparent contradiction may in part be due to immunodominant determinants on the envelope being physically separate from important protective and neutralizing sites.

Full-length and various truncated forms of the HIV *env* gene have been inserted into Baculovirus vectors and recombinant glycoproteins of 15,000 to 160,000 molecular weight have been expressed in insect cells. Of more than 600 sera from clinically-diagnosed AIDS patients, all had antibodies that recognized a recombinant gp150 polypeptide using an immunoblot assay. However, when measured by immunoblot, ELISA, and RIP assays many of these same sera had low or undetectable antibodies against a recombinant glycoprotein (gp120*) which represents more than 90% of the amino-terminal portion of HIV gp120.

Animals immunized with gp120* or recombinant HIV proteins that include this region of the envelope produced high titer antibodies that recognized the native viral envelope. Unlike the serum antibodies found in the human AIDS patients we tested, animal sera against these recombinant proteins have high titer antibodies against the portion of the envelope included in gp120*. Also, unlike most sera from AIDS patients, sera from animals immunized with these recombinant envelope proteins contains antibodies that neutralize HIV *in vitro* at high dilutions. Our data indicate that the apparent lack of a protective immunity in infected humans may in part be due to a misdirected immune response to the viral envelope.

W.3.5 CORRELATION OF CLINICAL STATUS AND NEUTRALIZING ACTIVITY OF SERA OF PATIENTS INFECTED WITH HTLV-III/HIV.
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Neutralizing activity (NA) in the sera of patients with AIDS, ARC, and the lymphadenopathy syndrome has been described extensively (Robert-Guroff 1985, Weiss 1985, Ho 1986, Rasheed 1986). Some investigators have found NA in sera of most patients with ARC (27/27,28/35 - Ho, Guroff) and AIDS (26/31,21/35), whereas others have found few AIDS sera possessing NA (Weiss, Rasheed). The role of neutralizing antibodies in preventing or retarding the progression of disease is of paramount importance in ascertaining the desirable target response of candidate vaccines. Indications that NA may play a beneficial role include the observation that 12/12 clinically stable children with AIDS, but only 1/12 children with a rapidly deteriorating clinical course exhibited NA in the serum (Robert-Guroff). We examined NA in a panel of sera, including a number of serial specimens, fom patients categorized according to the Walter Reed Staging Classification (Redfield 1986) against a number of viruses derived from molecular clones of HTLV-III/HIV (HX10, HXB2D, & others). We failed to find a significant correlation of the NA of individual sera against any clone or clones with respect to stage of disease (p=0.578,n=26), and found NA to differ substantially even between very similar strains. These results suggest that determining the clinical significance of the presence of NA against any single strain or closely related strains of HTLV-III/HIV may be difficult.

W.3.6 Group specific T cell response to HIV in chimpanzees immunized with external glycoprotein gp120 of HTLV-IIIB
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In a pursuit of an effective and safe HIV vaccine, chimpanzees were immunized with purified external envelope glycoprotein, gp120 from HTLV-IIIB, and the immune response towards HIV was monitored. Neutralizing antibodies were measured with the ATH-8 assay, based on the cytolytic effect of HIV on this target cell line. Cellular immune response was followed by T cell proliferation assay, IL-2 measurements and by assessing the capacity of immune lymphocytes to suppress the expression of HIV in cultures of infected autologous cells. All immune animals, but not the controls, showed an antibody response towards gp120 in Western blot. Neutralizing antibodies were strictly type specific to HTLV-IIIB. In contrast, T cell IL-2 production and proliferative response to whole heat killed virus was group specific, seen with three different HTLV-III isolates (B, MN, RF). The proliferating cells were CD-4 or CD8 +ve and -ve for B cell markers. When immune lymphocytes, stimulated with gp120 were added into cultures of autologous lymphocytes infected in vitro with HTLV-IIIB, the percentage of cells expressing viral antigens fell from 5-10% to 0-2%. The above results demonstrating group specific cellular immune response to HIV even when a vaccine candidate representing only one isolate is used raises hope for the development of a vaccine against HIV infection.

Blood and Blood Products—Screening and Donor Characteristics

W.4.1 Epidemiologic Characteristics of Blood Donors Who Have Antibody to the Human Immunodeficiency Virus
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The demographic and epidemiologic profile of donors with antibody to the human immunodeficiency virus (HIV) is useful for educating donors and studying the prevalence of HIV infection. We examined persons positive for HIV antibody who donated blood from March 1985 to July 1986 at three major U.S. blood centers. Of 818,629 donations, 450(0.05%) were HIV-antibody-positive; decreasing from 0.07% to 0.04% during the study period. When compared with seronegatives, HIV-seropositive donors tended to be 20-40 years of age (81%), male (88%), and black (47%). HIV seroprevalence among white donors (2/10,000 donations) was lower than among black (31/10,000 donations) ($p<0.0001$) and Hispanic (9/10,000) ($p<0.0001$) donors. Seventy-seven percent of seropositive males reported sexual contact with men; 41% were bisexual. Although 44% of seropositive females had apparently acquired infection from heterosexual contact, an equal percentage denied having risk factors for HIV infection. A small but decreasing number of HIV-infected persons continue to donate blood. Black and Hispanic communities may have an increased prevalence of HIV infection in donor populations and/or may have received less information concerning donor self deferral. The high proportion of bisexual men suggests these men may be unaware of their risk for infection. Donor education efforts should be targeted toward minority and bisexual men who may not consider themselves at risk for HIV infection.

W.4.2 Risk of HIV Transmission by Anti-HIV Negative Blood
STEVEN KLEINMAN, American Red Cross, Los Angeles, CA

Because anti-HIV does not develope until several months after HIV exposure, anti-HIV screening of donated blood is not expected to eliminate HIV transmission via transfusion. We have estimated this risk, by analyzing the results of anti-HIV testing of 676,000 donations (dona) over a 21 month period. We have found 17 donors (.003% of dona tested) who have had an anti-HIV(-) dona followed by an anti-HIV(+) dona. The intervals separating these dona were a) 3 months (mo) for 8 donors, b) 3 to 6 mo for 5 donors and c) 6 mo for 4 donors. We have tested 4 recipients of anti-HIV(-) blood from 3 Group A donors. Two tested anti-HIV(+), having received blood 2 and 4 months prior to the donor's seroconversion. Donors in Groups A and B gave 16 anti-HIV(-) units; with an assumed 50% infectivity rate, we estimate the risk of HIV acquisition from anti-HIV(-) blood to be 1 in 84,000.

When compared to anti-HIV(+) donors who did not seroconvert (n=323), seroconverting donors were less likely to be gay (44% vs. 86%, p=.01) and more likely to have possible heterosexual exposure or no identified risk (44% vs. 9%, p=.01). In late 1986, seroconverting donors comprised 14% of all anti-HIV(+) donors as compared to 2% in 1985 (p=.002) and 6% in early 1986 (p=.1). Our data suggests that the risk of HIV transmission from anti-HIV(-) units may increase unless donor deferral and screening methods are improved.

W.4.3 Serologic and Culture Follow-up Study of Anti-HIV Reactive Blood Donors

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As of December 1986, 473 donors had been repeatedly reactive by EIA for anti-HIV. Of these, 119 were Western blot positive (WB+), 334 were Western blot negative (WB-), and 20 were considered equivocal (WBeq) based on the presence of weak p24 and/or p55 bands only. We have enrolled 75 of these donors in 3 to 6 month follow-up studies. The initial and follow-up sera were tested by 6 different EIA screening tests for anti-HIV*, by 2 anti-HIV tests using recombinant antigens**, by 2 HIV-antigen assays**and by screening for anti-HLA antigens. Lymphocytes from WB+ and WBeq donors were cultured for HIV by standard techniques; cells from WB- donors were pooled prior to culture. Cultures were monitored by reverse transcriptase, in situ hybridization, in vitro DNA amplification***, immunocytochemistry, and HIV-antigen assay**.10/10 WB+ donors (7 with risk factors) were positive by all EIA and recombinant antibody assays on both samples, 2/10 had detectable plasma HIV-antigen, and HIV was cultured from 8/10. 50 WB- donors with both index and follow-up sera were negative by at least 7/8 antibody tests and by both antigen tests; HIV was not detected in pooled cultures from these donors; the majority tested had HLA antibodies. Whereas 11/15 WBeq donors were negative on all follow-up testing, 4 had persistent atypical antibody profiles; none were HIV culture positive. These results confirm persistent infection of most WB+ donors, and demonstrate the value of follow-up HIV test panels to clarify the status of WB-/eq donors. (Supported by NHLBI: 1-P01-HL36589-01; HB-6-7024).

*Abbott, Genetic Systems, Dupont, Burroughs-Wellcome, ENI, Chiron
**Abbott, Chiron ***Cetus

W.4.4 Characteristics of EIA and Western Blot Positive Blood Donors in a Multicenter Study

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In December 1985, a prospective study was begun at 11 geographically different blood collection centers in the U.S. to: (1) characterize risk factors of EIA-positive donors; (2) assess the EIA ratio as a predictor of Western blot (WB) status; and (3) determine the ability to isolate virus from EIA positive patients. Blood specimens from EIA positive donors were obtained for T-lymphocyte testing, WB analysis, and viral cultures. As of November 1986, 658 EIA positive donors were enrolled in the study. Of these, 52 (8%) were WB positive (34 males, 18 females), and 5 were culture positive. There were geographic differences in the proportion of EIA positive donors tested positive by the WB test. WB positive donors were more likely to have T4/T8 ratios below 1 than were WB negative donors (21 of 45 versus 31 of 521; $p<.0001$). WB positive males were more likely to have had sex with a male than WB negative males (18 of 33 versus 4 of 284; $p<.0001$). WB positive females were more likely to have a history of sexual contact with an IV drug user than WB negative females (3 of 13 versus 2 of 279; $p<.001$). Analysis of EIA OD ratios confirmed that higher ratios were better predictors of a WB positive test. These data indicate that individuals at risk for AIDS continued to donate blood at some centers during this period.

W.4.5 Human Immunodeficiency Virus (HIV) Cultured from Limiting Dilutions of the Peripheral Blood Mononuclear Cells (PBMC) of Asymptomatic Seropositive Persons

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To determine the prevalence of HIV infection in seronegative blood donors, we propose to culture the PBMC from 200,000 donors using pool sizes of 20-200 specimens. In this pilot study the proportion of HIV-infected PBMC from 10 asymptomatic anti-HIV(+) persons has been defined using two separate approaches: (1) Direct probing of the uncultured PBMC for viral nucleic acids and antigens using in situ hybridization (ISH) and immunocytochemistry (IC) analyses, respectively; (2) Limiting dilution of the HIV-infected PBMC in cocultures with PHA-stimulated normal PBMC assessed by reverse transcriptase (RT), ISH and IC. The dilutional studies revealed a higher proportion of HIV-infected cells ranging from 1:100 to 1:10,000 in comparison with exceedingly rare (less than 1:10,000) HIV-positive cells detected either by direct ISH or IC analyses. Thus, a large proportion of in vivo-infected cells are not producing detectable levels of HIV-RNA or proteins without in vitro stimulation in the coculture procedure, suggesting that they are latently infected and require in vitro stimulation for the expression of viral gene products. Because 10- to 10,000-fold dilution of HIV-infected PBMC coculture with normal PBMC leads to virus recovery, it may be possible for us to grow the virus out of HIV-infected cells from a single individual when mixed with cells from uninfected donors and the pool of 100 PBMC specimens is cocultured in an analogous procedure. (Supported in part by the NHLBI Contract HB-6-7024, Grant P01 HL-36589 andcarried out in conjunction with the SFMHS supported by NIAID Contract NO1 AI-32519.)

W.4.6 HIV Blood Screening in Africa: Are there no Alternatives?

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Screening potential blood donors using the presently available ELISA methods is not feasible in many African countries. To determine the percentage of HIV(+) blood donors which could be excluded by simple history and physical exams, we screened for HIV antibody and conducted physical examinations on all 325 blood donors (307 men and 18 women) who donated blood at Mama Yemo Hospital, Kinshasa, between March 3 to April 4, 1986. Sixteen (5%) donors (14 men and 2 women) were HIV(+) by ELISA and Western blot (a rate similar to the one previously observed in the adult population of Kinshasa). No significant differences in clinical findings or exposure to established HIV risk factors between HIV(+) and HIV(-) blood donors were found. Two-hundred and twenty-seven (70%) of 325 units would have been rejected if we had used the following exclusion criteria for screening blood donors: 1) paid donor 2) symptoms suggestive of HIV infection 3) abnormal physical examination 4) history of tuberculosis, herpes zoster or venereal disease within the past year 5) transfusions during the past 5 years 6) receipt of injections during the past 6 months. Of the 99 units not rejected by these criteria, one was HIV(+). Because of the persistent blood shortage in Africa such a high rejection rate is unacceptable.

Use of a lab test-independent clinical screening profile to reject high risk donors in Africa is not possible. An inexpensive, highly sensitive, rapid, simple machine independant laboratory test for detection of antibody to HIV is urgently needed.

Clinical Management—Pulmonary, Pediatric and Neurologic Implications

W.5.1 Predictive Value of Chest X-rays (CXR) for Lymphocytic Interstitial Pneumonitis (LIP)/Desquamative Interstitial Pneumonitis (DIP) in Pediatric Patients with AIDS

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LIP/DIP is the most common pulmonary disease in children with HIV infection. Currently, diagnosis requires biopsy (BX) of lung tissue. To evaluate the value of CXR in identifiying LIP/DIP, we compared pre-Bx CXR with pulmonary histopathology. 32 children (15 male, 17 female) with HIV infection underwent lung BX. Mean age at BX was 26.4 mos (3.5-120 mos). Medical records were reviewed to determine respiratory status, results of CXR and histopathologic diagnosis. All children presented with respiratory symptoms: rales>retractions cough>clubbing,>rhonchi>wheeze. Histopathologic results follow: 23/32 LIP/DIP; 7/32 Pneumocystis carinii pneumonia (PCP); 1/32 Cytomegalovirus (CMV) pneumonia 1/32 nonspecific inflammatory disease. Pre-BX CXRs were read by one pediatric radiologist. Nineteen of 32 CXRs had linear/nodular pattern (LN); 8/32 consolidation, and 5/32 were normal. Of patients with LIP/DIP, 18/19 had LN, 1/8 consolidation and 4/5 normal CXR. We evaluated LN CXR as a predictor of LIP/DIP. Sensitivity 0.78, specificity 0.89, positive predictive value 0.95, negative predictive value 0.62. When a second pediatric pathologist blindly read the same CXRs, sensitivity 0.52, specificity 0.78, positive predictive value 0.86, negative predictive value 0.39.

These data suggest that LN on CXR in this cohort is highly predictive of LIP/DIP. Further studies will be necessary to confirm these observations. Among HIV infected children with chronic respiratory symptoms, LN CXR may prove sufficient for diagnosis of LIP.

W.5.2 Retroviral antigenemia in children with HIV infection.

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A selected group of 35 children with suspected or documented HIV infection were tested for plasma HIV antigen using an ELISA antigen capture assay. Plasma from 33 of these were antigen positive at some time in their life. Antigen concentrations were determined in those with AIDS (range of 18-3026 pg/ml; mean $\pm$ S.D. of 573 $\pm$ 404); in those with ARC (range of 0-2143 pg/ml; mean $\pm$ S.D. of 499 $\pm$ 202); and those without symptomatology (range of 0-175 pg/ml; mean $\pm$ S.D. of 55 $\pm$ 213). The latter group had significantly lower HIV antigen levels than those with clinical illness. Two sets of HIV antibody positive twins were also antigen positive. One of each twin set developed severe HIV related illness in the first 4 months of life. Within each set, the affected twin had the higher titre of antigen. Plasma from 8 high risk maternal-infant (MI) pairs was assayed for HIV antigen at the time of delivery. Three antigen positive babies were born to antibody positive but antigen negative mothers. One MI pair was concordantly antigen positive and 1 MI pair was concordantly antigen negative. Three antigen positive mothers delivered antigen negative babies, however, 2 of these babies developed antigenemia at subsequent evaluations during the first year of life. These data suggest that (1) prenatal HIV infection may occur; (2) passive transfer of HIV antigen across the placenta need not occur; and (3) that natal infection with subsequent antigenemia is possible. All the children from the MI pairs are immunologically and clinically well to date but continued followup is necessary. HIV antigen testing of plasma may help explain patterns of vertical transmission of virus and possibly predict clinical manifestations of disease.

W.5.3 Pediatric AIDS: Neurologic Syndromes

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To further delineate the spectrum of central nervous system [CNS] syndromes in pediatric patients with HIV infection we have followed 63 infants and children [ages 6 weeks to 13 years] in an ongoing study. Forty-eight children had AIDS and 15 ARC. CNS dysfunction was documented in 61. Manifestations included microcephaly, cognitive deficits, encephalopathies and corticospinal tract signs. The neurologic course in 5 AIDS patients was rapidly progressive. Ten patients [9 AIDS, 1 ARC] had a subacute but steadily progressive course with loss of cognitive skills, progressive long tract signs and movement disorders. In 28 patients [25 AIDS, 3 ARC] the course was punctuated by plateaus during which no new milestones were attained. Cognitive assessments, revealed mild to severe mental retardation and long tract signs were common. Of these patients, 10 [9 AIDS, 1 ARC] had further neurologic deterioration. CT examinations revealed marked white matter abnormalities, cerebral atrophy and calcification of the basal ganglia. These CT findings correlated well with recovery of HIV from CSF, and with neuropathologic findings of myelin pallor, inflammatory responses with multinucleated giant cells, calcific vasopathy, and corticospinal tract degeneration. Six patients [4 AIDS, 2 ARC] with plateaus improved but remained mentally retarded. Eighteen patients [7 AIDS, 11 ARC] had a static encephalopathy: moderate to borderline mental retardation with varying degrees of stable motor deficits. CNS lymphoma, cerebrovascular accidents, and CNS infection by conventional pathogens occurred in 8 children [11%]. We conclude that [1] CNS involvement with progressive encephalopathy occurs frequently in children with HIV infection; [2] unlike adult AIDS patients, CNS opportunistic infections are uncommon; [3] In neurologically stable children, morbidity includes mental retardation.

W.5.4 Objective Clinical and Histological Prognsotic Factors for Patients with *Pneumocystis carinii* Pneumonia and the Acquired Immunodeficiency Syndrome.

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Pneumocystis carinii pneumonia (PCP) is the most frequent life-threatening opportunistic infection occurring in patients with the acquired immunodeficiency syndrome (AIDS). In this study, objective clinical and histopathological characteristics were analyzed to assess acute and long term prognostic significance in 43 patients with AIDS and PCP. Survival data, alveolar-arterial oxygen (A-a) gradients, clinically blinded graded chest radiographs and scored transbronchial biopsies were analyzed for all 43 patients.

Prognostic factors for survival for the acute episode differed from factors correlating with long term survival following the diagnosis of PCP. Thirty of 43 patients (70%) survived the acute episode. Decreased ability to survive the acute episode of PCP was associated with widened A-a gradients (>30torr) and more severe abnormalities on initial chest radiographs ($p<0.05$). Histopathologic specimens were semi-quantitatively scored for severity of 5 separate components of alveolar damage. Cox proportional hazards analysis revealed long term survival following the diagnosis of PCP correlated with the severity of edema on biopsy ($z=2.25$, $p<0.05$), and the extent of A-a gradient at the time of initial diagnosis ($z=2.88$, $p<0.05$).

Repeat bronchoscopy with re-biopsy was performed in 27 of the 43 patients following an average of 3 weeks of therapy. The persistence of pneumocysts on follow-up bronchoscopy was associated with significantly decreased long term survival ($p<0.05$ at 8 months following the diagnosis). Patients diagnosed more recently (July 1985-July 1986) has less severe pulmonary disease at the time of diagnosis (possibly due to earlier, more aggressive evaluation) by the parameters examined in the study and a better prognosis for survival the acute episode ($p<0.05$) than patients diagnosed earlier (January 1983 to June 1985).

Thus, important prognostic information can be derived from objective clinical and histopathologic data obtained at the time of diagnosis and at follow-up bronchoscopy in patients with AIDS and PCP. The improved survival in patients with less severe disease as measured by these objective paramcters suggests that early detection and therapeutic intervention for patients with PCP may improve chances for survival.

W.5.5 Serum Lactate Dehydrogenase levels (LDH) in Pneumocystis carinii pneumonia (PCP) in AIDS: Possible Indicator and Predictor of Disease Activity.

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Seventy-eight AIDS patients with first episode PCP and moderately well (95% had $pO_2 \geq 60$) had LDH determinations on days 0,1,3,6,14,18,21, one and 2-3 months after end of treatment. During the acute phase significant elevation of serum LDH activity was noted in all patients. The LDH followed a specific pattern beginning to increase one week prior to diagnosis; the peak was usually on day 6 to 8 and declined to normal levels within one and a half months. In 67 patients with good outcome (survivors without respiratory failure) the mean initial LDH was 355.9 U (150-520). Eleven patients had a poor outcome (respiratory failure or death w/o intubation); the initial LDH was significantly higher in these patients with a mean value of 710 (450-977). All the survivors with or without respiratory failure showed a decline in LDH levels after 5-6 days of therapy. All nonsurvivors had a progressive increase in their LDH levels after day 6 to 8. LDH isoenzymes were performed in 19 patients. In all but 2 LDH fraction 3 was abnormally elevated (↑26%).

These findings suggest that serum LDH activity is a useful indicator of the severity of PCP in AIDS patients and that it may be utilized to predict disease course and monitor response to treatment.

W.5.6 Serum Glutamic Acid as Potential Marker for Pneumocystis carinii Pneumonia in AIDS.

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Current diagnostic techniques, open lung biopsy and bronchoscopy, are highly invasive and cannot be used to monitor therapy. Objective: to find a circulating serum marker that could be used repeatedly for both diagnosis and monitoring. Identification: computer comparison of gas chromatographic-mass spectrometric (GC-MS) profiles of the trimethylsilyl (TMS) derivatives of aqueous extracts from PCP invaded lungs and normal lungs revealed a potential marker, the presence of which was also confirmed in PCP serum samples. The marker was identified as L-glutamic acid (glu) by both low and high resolution mass spectrometry (electron and chemical ionization) using TMS and acetyl-methyl derivatives and also by using L-glutamic decarboxylase to remove glu. Quantification in serum: GC-MS (int. std.: deuterated glu); analyses were also made using colorimetry and liquid chromatography. Glu conc. >108 uM (mean of normal +2s.d.) considered elevated. Of 103 patients (70 coded) containing 73 independently confirmed PCP cases (45 coded) sensitivity: 81%, specificity: 86%. Of 22 patients with blood taken within 3d of bronchoscopy: 15 of 20 with proven PCP were positive. Two true negatives and 5 PCP cases were negative. No false positives were found. This suggests that invasive testing need be performed only in those who do not have elevated glu conc. Preliminary results revealing concurrent changes in serum glutamine (gln) conc. suggest that chenges in glu may result from physiological changes caused by PCP, resulting in an altered glu/gln ratio.

(Supported by AIDS Institute, State of New York, and the I.G. Martell Memorial Foundation for Leukemia and Cancer Research).

Roundtable Discussions

W.6

Heterosexual Transmission of the AIDS Virus

Panel Organized By: Dr. Tim Dondero
Centers for Disease Control
Atlanta, Georgia

H. Hunter Handsfield, Seattle-King County Department of Public Health and University of Washington, Seattle, Washington

Peter Piot, Institute of Tropical Medicine, Antwerp, Belgium

Robert Redfield, Walter Reed Army Institute of Research, Washington, D.C.

Niel Stelgbigel, Montefiore Medical Center, Bronx, New York

Rand Stoneburner, New York City Health Department, New York, New York

W.7

Vaccine Related Issues

Panel Organized By: Gerry Quinnan
Food and Drug Administration
Bethesda, Maryland

Patricia Fultz, Centers for Disease Control, Atlanta, Georgia

Fritz Deinhardt, Max v. Pettenkofer-Institut, Munich, Federal Republic of Germany

Dani Bolognesi, Duke University Medical Center, Durham, North Carolina

John La Montagne, NIAID, Bethesda, Maryland

Richard Kaslow, NIAID, Bethesda, Maryland

W.8

Legal, Ethical and Public Policy Issues:
The American Perspective

Panel Moderator: Gene Matthews
Legal Advisor
Centers for Disease Control
Atlanta, Georgia

Earl Shelp, College of Medicine, Houston, Texas

June Osborn, University of Michigan, Ann Arbor, Michigan

Carol Levine, The Hastings Center, Briarcliff Manor, New York

Harold Edgar, Columbia University School of Law, New York, New York

Joan B. Campbell, World Council of Churches, New York, New York

Alvin Novick, Yale University, New Haven, Connecticut

Larry Gostin, American Society of Law and Medicine, Boston, Massachusetts

W.9

Assuring an Adequate Blood Supply of Healthy Blood Donors
in This Age of AIDS

Panel Organized By: Gerald Sandler
American Red Cross
Washington, D.C.

Gordon T. Archer, Australian Red Cross, Sydney, New South Wales, Australia

Richard E. Counts, Council of Community Blood Centers and Puget Sound Blood Center and Blood Program, Seattle, Washington

Lewellys F. Barker, International Society of Blood Transfusion and American Red Cross National Headquarters, Washington, D.C.

Joseph R. Bove, American Association of Blood Banks and Yale-New Haven Hospital, New Haven, Connecticut

Anthony F.H. Britten, League of Red Cross and Red Crescent Societies, Geneva, Switzerland

Jonathan Mann, World Health Organization, Geneva, Switzerland

W.10

Meeting Gaps in Medical Needs

Panel Moderator: Reed Tuckson
Commissioner of Public Health for
the District of Columbia
Washington, D.C.

Joseph A. Nkwanyuo, Internal Medicine, Baltimore, Maryland

Elmer W. Smith, Health Care Financing Administration, Baltimore, Maryland

Paul A. Volberding, San Francisco General Hospital, San Francisco, California

James M. Graham, Whitman-Walker Clinic, Inc., Washington, D.C.

A Representative of the Robert Wood Johnson Foundation

Poster Session

WP.1

Enhanced In Vitro Suppression of HIV Infectivity by a Combination of Nucleoside Analogs

LIONEL RESNICK*, A. M. MIAN**, *Mount Sinai Medical Center, Miami Beach, FL, **University of Miami School of Medicine, Miami, FL.

Azidodeoxythymidine (AZT),a nucleoside analog with anti-HIV reverse transcriptase (RT) activity in vitro has been found to have clinical toxicity that limits drug dose. 6 thio-deazaguanine (6TOG),a nucleoside analog with antiviral properties,was tested individually and in combination with AZT to determine if HIV inhibitory activity occurred in vitro. A drug screening assay was developed to evaluate the antiviral activity of compounds at drug levels causing no target cell cytotoxicity over a broad range of multiplicity of infectious units (MOI) and over prolonged periods of time. Evidence of HIV infection and replication in culture was monitored by RT assays,immunofluorescense cellular assays with anti-p24 monoclonal antibody and cell-cytopathic effects. At an MOI of 1,AZT (2ug/ml) and 6TOG (0.3ug/ml) individually exhibited suppressive effects on HIV expression throughout the 20-day experiment. The HIV infected culture without drug (control) revealed the presence of HIV on day 10. At an MOI of 100,HIV replication was detected at day 10 with 6TOG (0.3ug/ml), day 20 with AZT (2ug/ml) and day 14 with AZT (1ug/ml) (control-presence of HIV on day 7). The utilization of AZT (1ug/ml) and 6TOG (0.1ug/ml) in combination,at lower doses,achieved complete suppression of viral replication at an MOI of 100 over the 20-day period. The combination of nucleoside analogs,AZT and 6TOG,appear to enhance the inhibition of HIV infectivity in vitro. Combination antiviral therapy may be important in maintaining efficacy at non-toxic drug levels.

WP.2

In Vitro Infection of Glial Cells with Diverse HIV Isolates

JONATHAN WEBER*, E. ROBEY**, R. AXEL**, R. WEISS*, *Chester Beatty Laboratories, Institute of Cancer Research, London, **College of Physicians and Surgeons, Columbia University, New York, 10032.

The susceptibility to HIV infection of 6 established malignant glioma cell lines was investigated, using a diverse range of characterised HIV isolates. The results were contrasted with the susceptibility of 50 primary cultures from malignant glioma tissue. One line, U 138.MG (Westermark) was susceptible to infection with diverse characterised HIV-I and HIV-2 isolates, including HIV RF, HIV IIIb, HIV RUT and LAV-2. Infected cells do not demonstrate indirect immunofluorescence for HIV antigens, and cultures were negative for antigen expression (Dupont), and only occasionally positive for reverse transcriptase; however, infected cells consistently produced syncytia with a T-cell line, C8166, which were specific for HIV. There was no evidence of the CD4 antigen on the cell surface, or in the cytoplasm, in infectable cells by immunofluorescence with several monoclonal anti-CD4 antibodies. However, CD4 mRNA was detected in these cells by northern blot with a CD4 probe; even so, it was not possible to block infection of glial cells with anti-CD4 monoclonals. The infected glial cells were not lysed by HIV, and grew normally. The possibility remains that HIV infected glial cells may be a target for lymphocyte cytotoxicity in vitro, and data on this will be presented.

WP.3

Persistent HTLV-IIIb and LAV Infection in Chimpanzees. Its Effect on Virus Biochemistry and Serology.

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The chimpanzee has been shown to be capable of persistent infection by HTLV III/LAV. This state of persistent viral infection can thus be utilized for biochemical and serological investigations. Three chimps were given either HTLV-IIIb-infected cells (#525), HTLV-IIIb virus only (#525), and LAV from a previously infected animal (#524). Virus was reisolated from all animals 1 1/2 years later and purified viral envelopes were compared to the original virus inoculum by oligo-chymotryptic peptide mapping methods. In the 2 cases where the original isolate was mapped (HTLV-IIIb), a difference in 2 peptides was detected in the reisolated virus. Viral maps from the LAV animal were similar to the reisolated HTLV-IIIb maps suggesting a host-induced modification. All animals developed progressively high titered, initially type-specific, neutralizing antibody response which progressively broadens after 2-4 months to a group-specific response. Maximal titers were found between 1 and 2 years following virus inoculation. Also, virus reisolated from each chimp was neutralized by each others sera, as well as their own. All animals' sera contain antibodies which recognize p24, Ag 121, gp120, and exhibit antibody-dependent, complement-mediated cytolysis (ACC). Human sera from healthy AIDS and ARC patients were found to be negative for ACC. Thus, it appears that chimpanzees persistently infected by one virus isolate undergo an in vivo expression to yield alternate form(s) of the envelope which leads to a group-specific response. Research sponsored, at least in part, by the NCI, DHHS, under Contract Number NO1-CO-23910 with Program Resources, Inc.

WP.4 Membrane Immunoassays for the Detection of HIV Antibody and Antigen

CELIA M. CRANE and KEVIN J. REAGAN, Medical Products Dept., E. I. Du Pont de Nemours and Co., Inc., Glasgow Research Laboratory, Wilmington, DE 19898.

The likelihood of HIV transmission through donor blood has been greatly reduced by the introduction of enzyme immunoassays (EIA) which monitor the presence of antibody to virus. In addition to an antibody assay, Du Pont has released as a research product an EIA designed to detect HIV core antigen. These assays are highly sensitive though their requirement for automation limits their application to modern clinical or research settings. Studies were initiated to adapt several methods to membrane surfaces designed to function without automation yet provide sensitive and specific detection of HIV antibody and antigen.

HIV antibody was monitored using two recombinant proteins, one specific for a portion of the viral envelope (gp41) and the other for core (p17,24,15). The recombinant antigens were placed on separate areas of a nitrocellulose strip. Diluted patient samples were incubated with the strips, and bound antibody was detected using alkaline-phosphatase-conjugated anti-human antibody and bromo-chloro-indolyl phosphate/nitroblue tetrazolium substrate. Excellent sensitivity was noted in a 40 minute assay using a visual read-out.

HIV antigen was monitored by sandwich immunoassays on nylon membranes. Two assays were devised, one to detect the major core protein, p24, and the other to detect envelope glycoproteins, gp120 and gp41. Measurement of p24 has been the more sensitive method with a detection limit of approximately 0.3ng/ml of p24. Nylon membranes having a large surface area permit a high concentration of capture IgG as well as dynamic sample flow-through.

WP.5 Development of clonal cell lines from Kaposi's sarcoma (KS) lesion (AIDS-KS) and their biological properties

ZAKI SALAHUDDIN*, S. NAKAMURA*, P. BIBERFELD**, and R. GALLO*. * National Cancer Institute, Betheda, MD. ** Karolinska Institute, Stockholm, Sweden.

AIDS-KS is an aggressive disease of young people and has a multifocal and histologically complex nature. So far, its origin and pathogenesis remain unknown, in part due to the lack of in vitro long-term culture system to produce large quantities of cloned cells. We report the isolation of KS cells, their long-term culture and their morphological and biological characteristics. They were isolated and cloned from KS lesions obtained from the lung of AIDS-patients. These cells gave only a low response to classical endothelial cell growth factors. However, conditioned medium from HTLV-II-transformed cell lines(HTLV-II-CM) supported the growth of KS cells for over 9 months and large quantities were harvested for study. Immunocytologically and morphologically, they shared the properties of lymphatic endothelial cells. CM from these KS cells(KS-CM) were tested for activity on normal endothelial(NE) cell growth, IL-1, colony stimulating activity and other growth factors. KS-CM promoted NE cell growth and it also had some effect on KS cell growth. NE cell growth promoting activity in KS-CM differes from HTLV-II-CM. Molecular analysis suggested similarity between basic fibroblast growth factor and KS-CM but not with HTLV-II-CM. It also contained IL-1-like factor as measured by thymocyte co-mitogenic assay. Because IL-1 could stimulate KS cell growth, it was suggested that a autocrine mechanism of the IL-1-like factor was related to KS cell growth. KS-CM has a potent neo-angiogenic activity. KS cells also induce KS like lesion, when they are transplanted in athymic nude mice. No viruses have been detected in cultured KS cells. In summary, our results are consistent with the idea that pathogenesis of KS may depend on the production and response to soluble factors.

WP.6 Role of synthetic peptide analogs of HIV on T-lymphocyte cells and on virus replication.

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Biological activity of HIV proteins is being studied by examining the effect of synthetic peptide analogs on lymphocyte proliferation and on virus replication in T4+ cell lines. Synthetic peptides from gp120 (aa 2-13, 55-65 and 192-200), from gp41 (aa 582-596, 579-600, 659-670, and 766-778), and from ptat (aa 46-58 and 60-72) were synthesized using the Merrifield procedure with COOH-terminal cysteine residues. One gp120 peptide (192-200) has been found to be a potent inhibitor of virus replication for isolate HTLV-IIIb (PNAS, 83, 9254-8, 1986) and a gp41 peptide (582-596 and extended peptide 579-600) has been found to be highly antigenic (PNAS, 83, 6159-63, 1986). Additionally the latter peptide has sequence homology to other retroviral transmembrane proteins that are known to suppress lymphocyte proliferation (Science, 230, 453-5, 1985). Our results indicate that peptides 582-596 and 579-600 both suppress lymphocyte proliferation with all other peptides having little or no effect. Replication in T4+ cell lines of an Australian isolate, in the presence of the above peptides, was compared with that of HTLV-IIIb. The results indicate variable effects on virus replication. Thus these regions in gp120, gp41 and/or ptat proteins may play important roles in virus replication at least 'in vitro'.

WP.7 MT-4 Plaque Assay Distinguishes HIV Serotypes and Distinct Biologic Isolates

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The MT-4 plaque assay, as described by Harada et al (Science 229:563, 1985) was used to quantitate infectious HIV. Six out of fourteen HIV isolates tested formed plaques. Titers were in the range of 5×10^3 to $2.5\ 10^5$ pfu/ml. Plaque formation did not correlate with ability of the fourteen HIV to replicate in established cell lines. Studies with the plaque-forming HIV isolates indicated the presence of neutralizing antibodies in many HIV-positive individuals. Neutralizing antibody titers as determined by the MT-4 plaque assay correlated well with those determined by reduction in reverse transcriptase acitivity in infected cells. The presence of these antibodies did not reflect a particular disease state.

During this study, it was noted that HIV_{SF2} did not form plaques in MT-4 cells. However plaqueswere induced by both HIV_{SF13}, an isolate obtained 5 months later from the same individual yielding HIV_{SF2}, and HIV_{SF2A}, an isolate recovered from a chimpanzee inoculated one year previously with HIV_{SF2}. The results of these studies suggest biologic changes in HIV over time in the same individual and in a new host. Comparative serologic studies and restriction enzyme and envelope gene analyses of HIV_{SF2}, HIV_{SF13}, and HIV_{SF2A} should indicate the extent of antigenic and molecular changes that have occurred in these HIV isolates.

WP.8 Cyclosporine A (CSA) prevents infection of healthy T cells by HIV but has no effect on pre-infected cells

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In order to determine the effect of CSA on ability of HIV to infect healthy peripheral blood lymphocytes (PBL's), these cells were stimulated with PHA for 48 hr, after which they were co-incubated with an excess of the $HTLV\text{-}III_B$ strain of HIV, in the presence of polybrene (2µg/ml). CSA (0.5µg/ml) was added to cultures after either 2 hr, 24 hr, or 72 hr. Infection of cells was monitored both by an indirect immunofluorescence assay, using monoclonal antibodies against viral proteins p15 and p24 and by measuring reverse transcriptase activity. In control cultures, untreated with CSA, the percentage of positive cells after 5 days was about 25%. The addition of CSA at 2 hr completely prevented viral infection in PBL's over 21 days. However, if the addition of drug was delayed either 24 hr or 72 hr after infection, the results showed that 1% and 15% of PBL's became positive for viral antigens after 12 days and 5 days respectively. CSA had no effect on the ability of $HTLV\text{-}III_B$-infected T cell line, H-9 cells, to replicate or to express viral antigens. HIV was able to infect PBL's obtained from each of 6 kidney allograft recipients on long-term CSA anti-rejection therapy, as long as CSA was not included in the culture medium. In addition, we were able to repeatedly isolate HIV from patients entered into a Canadian therapeutic protocol, in which CSA was used to treat AIDS patients with advanced disease. Supported by Health and Welfare Canada and by the Medical Research Council of Canada

WP.9 Correlation of Serum HIV Antigen Detection with Isolation of HIV from Patients with AIDS and Patients at Risk for AIDS.

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HIV isolation was attempted with peripheral blood mononuclear cells (MNC) from AIDS patients (n=41), ARC patients (n=28), HIV seropositive asymptomatic homosexual males (AHM) (n=37), and HIV seronegative AHM controls (n=29). All samples were obtained from individuals who were hospitalized or seen by a private physician. Cultures were performed using peripheral blood MNC from healthy heterosexuals which were stimulated with PHA (PHA-MNC) and cocultured with MNC of the above patient groups after addition of IL-2 and polybrene to the medium. Virus was isolated from 39 of 41 AIDS (95%), 16 of 28 (57%) ARC, and 22 of 37 (59%) asymptomatic antibody positive homosexual males. All control patients were culture negative. The association between HIV-Ag detection and virus isolation is shown in the following table:

HIV	Culture Results Among Patient Groups					
	AIDS		ARC		AHM	
p24 Ag	Pos	Neg	Pos	Neg	Pos	Neg
+	18	0	12	3	15	2
-	21	2	4	9	7	13

There was no significant association noted between detection of HIV-Ag and virus isolation among AIDS patient. In contrast, there was a significant association ($p \leq 0.01$) between HIV-Ag in serum and positive cultures among ARC and AHM patients. Detection of HIV-Ag in the serum of patients with ARC or asymptomatic HIV antibody positive individuals may be predictive for isolation of HIV from MNC.

WP.10 DETECTION OF DIFFERENT TYPES OF OLIGOSACCHARIDES IN ENVELOPE GLYCOPROTEINS OF HIV/HTLV-III VIRUS

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The envelope (Env) structures of the HIV/HTLV-III virus (gp160,gp120) have been defined as glycoproteins on the basis of their ability to bind Lens Culinaris Lectin (LCL), incorporate radiolabelled glucosamine in cell cultures, and display a significant reduction in their molecular weight following treatment with endoglycosidases. The deduced amino acid sequences of several viral isolates indicates the presence of 28-30 potential N-linked glycosylation sites (Asn-X-Ser/Thr) within gp160; of these, approximately half are located with invariant regions of the polypeptide chain. The purpose of our experiments was to determine what types of oligosaccharides are linked to HIV/HTLV-III Env glycoproteins. Cell-free supernatants obtained after centrifugation of cultures of HIV/HTLV-III infected cells at their peak of reverse transcriptase activity, and Env glycoproteins isolated by micro immuno-affinity chromatography, were subjected to SDS-PAGE, electroblotted onto nitrocelluiose, and probed with a panel of biotinylated lectins of well defined carbohydrate binding specificity. Lectin binding was determined before and after exo- and endoglycosidase treatment of virus components. Gp160 and gp120 bound Con A, LCL, PSA, PHA-E and LFA. This binding patterns suggests that oligomannosyl, as well as nonbisected fucosylated and sialylated biantennary oligosaccharides are present in both glycoproteins. Binding of PHA-L was weak. Binding of PNA to gp120 after desialylation, and absence of binding after alkaline hydrolysis suggests the presence of sialylated O-linked Gal-GalNac sequences within this glycoprotein. Binding of lectins to gp41 was consistently weak. Experiments are in progress to study the possible role of gp120 oligosaccharides in the binding of HIV/HTLV-III to the T4 receptor molecule.

WP.11 Genetic Variation of the AIDS Virus In Vitro

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Human immunodeficiency virus (HIV, HTLV-III/LAV) isolates from different individuals have been found to exhibit striking genetic diversity. It is unclear, however, to what extent these sequence changes reflect variation that has occurred in vivo as compared to in vitro. To address this question, we compared the restriction pattern of HIV from uncultured brain tissue with that of virus from the same brain tissue cultured in peripheral blood lymphocytes and H9 cells. 12/12 restriction fragments generated by 4 different endonucleases were identical in the cultured and uncultured specimens. A second approach to assessing the relative rate of viral genetic variation in vitro was to subject virus to repeated rounds of cell-free terminal dilution followed by expansion in H9 cells, thus forcing multiple rounds of viral replication and reverse transcription. Sequential terminal dilutions of virus isolate WMJ-1 over a five month period gave rise to five virus isolates, WMJ-1(TD-1) to WMJ-1(TD-5). WMJ-1(TD-5) infected H9 cell DNA had an identical HIV restriction pattern to the original parental isolate WMJ-1 for all 6 restriction enzymes tested (Sst I, Eco RI, Hind III, Bgl II, Pst I, Pvu II) indicating that the predominant viral species had not changed. Furthermore, 10 out of 11 full-length HIV/λ phage clones derived from WMJ-1(TD-5) were identical to the parental WMJ-1 isolate. These data demonstrate that the striking genetic diversity observed in independent HIV (HTLV-III/LAV) isolates results from mutations that have occurred in vivo, not in vitro. Since the magnitude of the genetic changes that occur in vivo is much greater than that observed in vitro, it is possible that genetic variation may be selected by host immune pressures.

WP.12 Epitope Mapping of the HIV gP120 Antigen Using Monoclonal Antibodies and Lambda gt11 Library Screening

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Although a small number of epitopes of the HIV envelope antigen have now been mapped, there remain several critical regions of the molecule whose locations are unknown. In particular, epitopes which may be responsible for interaction with the virus receptor, the CD4 antigen, have yet to be delineated in the envelope protein. In order to begin such an analysis, a collection of monoclonal antibodies against the gp120 antigen has been developed. Seven monoclonal antibodies (MAbs) from heterologous rat-mouse and ten MAbs from mouse-mouse hybridomas were generated against a recombinant form of the gp120 glycoprotein (rgp120) from the human immunodeficiency virus strain 111b. All seven of the rat-mouse MAbs, and three of the mouse-mouse MAbs, reacted with intact rgp120 and a 75,000 Dalton amino terminal proteolytic fragment by Western blot analysis. In addition, three other mouse-mouse MAbs bound to a 55,000 Dalton proteolytic fragment corresponding to the carboxy-terminus of rgp120. Competition analysis of the various MAbs has allowed them to be placed into seven different groups.

In order to map the location of the epitopes recognized by these MAbs, a collection of small, random DNA fragments from the gp120 gene has been incorporated into a lambda gt11 expression vector. Screening of this library with the various MAbs, as well as with polyclonal serum from patients, has resulted in the mapping of epitopes recognized by these MAbs as well as by the immune system of an infected individual. The location of these various epitopes will be presented.

WP.13 Use of PHA Can Interfere With Efficient Recovery of HIV From Periperal Blood Mononuclear Cells.

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Methods for isolation of the human immunodeficiency virus (HIV) from peripheral blood mononuclear cells of HIV-seropositive individuals vary among laboratories, but usually involve mitogenesis with phytohemagglutinin, or addition of normal allogeneic PMC from HIV seropositive blood donors. Using PHA as a stimulus, we can routinely recover HIV from the PMC of about 50% of healthy HIV-seropositive subjects, and from 75-90% of those with AIDS or ARC.

We have undertaken studies to determine if PHA and allogeneic lymphocytes function equally well in virus isolation, or if some combiation of the culture methods should be used to optimize recovery of HIV. Two sister cultures established from the PMC of 11 HIV seropositive subjects received either (1) medium containing PHA (3ug/ml), or (2) medium without PHA, but with $6x10^6$ normal human PMC previously stimulated with PHA. All cultures were passed without PHA every 3-4 days and received normal PMC after day 9 as required. Culture fluids were assayed after day 7 for reverse transcriptase activity.

Virus was recovered from 6 of the 11 subjects. Of these, 5 released virus only when their PMC were cocultured with normal PMC and not PHA. One subject released virus when his PMC were cultured with either PHA or normal PMC. These results suggest that recovery of HIV from seropositive subjects can be improved by co-culturing the PMC with allogeneic PMC from HIV-seronegative blood donors without the use of PHA. It is conceivable that CD4+ cells in the normal PMC population act as additional targets for virus replication, or that the presence of PHA in the culture supernatant stimulates the generation of cells with antiviral activity. These possibilities are under investigation.

WP.14 Identification of HIV Serotypes with Distinct Patterns of Sensitivity to Serum Neutralization

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The Human Immunodeficiency Virus (HIV) displays a high degree of genetic variation, especially in the gp120 domain of the env gene. To determine whether this genomic heterogeneity leads to the expression of different independent HIV serotypes, twelve HIV-positive sera were tested for their ability to neutralize infection of peripheral mononuclear cells (PMC) by a panel of diverse HIV isolates. The HIV used included those from the United States, Dominican Republic and Africa. Some of these HIV were isolated from nerve tissues.

Results show that the isolates can be grouped into three distinct classes:
A) those neutralized by all sera tested at high titers,
B) those neutralized by only certain sera at low titers, and
C) those neutralized by none of the sera.
No correlation was observed between the ability of patient's sera to neutralize HIV infection and serum anti-env or IFA titers or severity of disease. The data define the presence of distinct HIV serotypes and suggest that for vaccine development, further characterization of HIV serotypes and their use in combination may be required.

WP.15 Trans-activation by STLV-3 and HTLV-4

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Simian T-lymphotropic virus type-3 (STLV-3) and human T-lymphotropic virus type-4 (HTLV-4) are closely related to the human immunodeficiency virus (HIV) yet evidently differ from HIV in their pathogenic potential in their respective hosts. As a step in understanding the biological differences between HTLV-4/STLV-3 and HIV we examined whether HTLV-4 and STLV-3 encode transactivator (tat) proteins which mediate gene expression from their long terminal repeats (LTRs). Chimeric genes were constructed consisting of HTLV-4 or STLV-3 LTRs joined to the protein coding region of the bacterial chloraphenicol acetyltransferase (CAT) gene. Additionally, DNA fragments containing either the first exon or both exons of the putative tat genes of both HTLV-4 and STLV-3 were placed under the transcriptional control of the SV40 early gene promoter. Co-transfection experiments and subsequent CAT enzyme assays and Northern blot analyses indicated that, like HIV, both HTLV-4 and STLV-3 encode trans-acting regulatory factors which increase gene expression from either HTLV-4 or STLV-3 LTRs. However, unlike HIV, trans-activation by HTLV-4 or STLV-3 is greatly enhanced by sequences extending beyond the first coding exon of the tat gene. The tat-mediated increase in gene expression was reflected by concommitant increases in both CAT RNA and protein.

WP.16 Genetic Analysis of *cis* and *trans* Elements Involved in the Regulation of HTLV-III.

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The genomes of HTLV-III and closely related viruses are unique in their possession of several novel genes not found in any other retroviruses. These include the *tat* and *art* genes, whose products play crucial roles in regulating viral protein expression, and the *sor* and 3' *orf* genes, whose functions remain unclear. Recently an additional novel gene has been identified in HTLV-III, encoded within an open reading frame designated the R region - preceeding the *tat* gene. Recent results will be presented from an ongoing systematic mutational analysis of elements involved either *cis* or *trans* in the regulation of the virus. Regions being investigated include the 3' *orf* gene, the R region, and the *art* gene product.

WP.17 Differential Recognition of HTLV-III/HIV Envelope Antigens is Correlated with Clinical Outcome

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Two types of antigenic domains are identified on HTLV-III/HIV envelope protein, gp120. One, designated gp120(N), requires the presence of disulfide bonds to maintain their antigenicity, while the other, designated gp120(R), does not. Analysis of 135 coded serum samples from patients who have been clinically staged by a Walter Reed staging classification system reveals that patients with AIDS (WR6 stage) are three times less likely to have antibody to gp120(R) than patients with just lymphadenopathy (WR2 stage). In contrast, all 135 patients had detectable antibody to gp120(N). This observation raises the possibility that differential response to different antigenic epitopes may have prognostic value and that gp120(R) may be more likely to elicit protective immunity than the more native gp120(N).

WP.18 Approach to Development of an AIDS Vaccine Using HGP-30, a Synthetic p17 Peptide Analogue

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Antisera against HGP-30 (HIV synthetic p17 gag peptide analogue — 30 amino acids), prepared by solid phase peptide synthesis, as well as antisera against thymosin α_1 ($T\alpha_1$) are highly effective in neutralizing the AIDS virus *in vitro*. Neutralization is defined as inhibition of viral growth in H9 infected human cells assessed both by measurement of reverse transcriptase and viral antigens (p17 and p24). HGP-30 contains a region of homology with p17 from position 86 to 115. The HGP-30 antisera is not significantly cross-reactive with $T\alpha_1$. When coupled to KLH, the antigen is highly immunogenic and effective in generating serum antibodies to HGP-30 as well as HTLV-IIIB p17. Used with either alum or complete Freund's adjuvant, the vaccine is immunogenic but not toxic in mice, rabbits, dogs and primates. The demonstration that antibodies to HGP-30 are neutralizing and cross-react with p17 provides a new and potentially more specific candidate for development of an AIDS vaccine. Using HGP-30, a small synthetic peptide, as the immunogen in a vaccine against AIDS offers the advantages of 1) ease of large-scale preparation and uniformity of a chemically defined product, 2) safety; does not require use of killed or attenuated virus, virus-infected cells or genetically manipulated products, 3) overcomes the problem of genetic drift; in contrast to env proteins the p17 epitope identified is highly conserved.(Supported by grants and/or gifts from the NCI (CA24974), Alpha 1 Biomedicals, Inc., and Viral Technologies, Inc.)

WP.19 SIV/Delta Induced SAIDS in Rhesus Monkeys: Pathogenesis of Cultured Isolates of Rhesus and Mangabey Monkey Origin.

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As a part of a tissue transmission study, we documented the association of an HIV-related retrovirus, SIV/Delta, with simian AIDS (SAIDS) in rhesus monkeys. Indirect evidence suggested that the origin of SIV/Delta in the rhesus, a primate of Asian origin, was an African primate, the sooty mangabey monkey, which may harbor this virus asymptomatically.

More recently, we have examined SIV/Delta-related pathogenesis of *in vitro* propagated virus isolated from several rhesus with SAIDS and one asymptomatic mangabey. SIV/Delta isolated from a healthy sooty mangabey monkey is as pathogenic in rhesus monkeys as are SIV/Delta rhesus isolates. Death due to SAIDS, evidenced by lymphocyte subset alterations, abnormal immune responsiveness, opportunistic infection, and lymphoma in one animal, usually occurs in infected animals within 2-12 months post-inoculation, regardless of the source of virus. Several rhesus isolates are pathogenic; one isolate is singularly neurovirulent. Of 8 animals inoculated with the neurovirulent isolate, 4 have died with symptoms of SAIDS; in addition, all had retroviral encephalitis evidenced by numerous syncytial cells in brain tissue. Long-term *in vitro* propagation of SIV/Delta may result in a loss of pathogenicity. Virulence may be re-established, however, by passage of the attenuated virus from an infected healthy rhesus monkey to a second animal. A comparison of the genetic and antigenic composition of these isolates will provide invaluable information on viral factors responsible for pathogenesis and neurovirulence.

WP.20 Packaging defective mutants of HTLV-III/HIV

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Although much is known about HTLV-III replication and the processing of structural components (gag, pol and env) in infected cells, the precise mechanism by which genomic viral RNA is preferentially packaged into virion particles is not known. Studies in avian and murine retroviral systems have suggested that (i) virus particle formation can occur in the absence of genomic RNA and (ii) that sequences intervening the 5'LTR and gag gene are crucial for virus specific packaging. To see whether analogous sequences in HTLV-III/HIV are important in selective packaging of HTLV-III genomic RNA and hence enable the construction of empty (non viral RNA containing) particles, we produced a series of mutants of the biologically active molecular clone pHXB2-D(HTLV-III_B). These mutants were deleted of 10 to 50 base pairs in the region bordering the 5'LTR and gag. Four such clones were studied in detail and shown to generate viral proteins and viral particles (morphologically indistinguishable from wild type) upon transfection into cos-1 cells. In contrast to the wild type virus, virus generated from the mutant clones was either poorly infectious (3 clones) or resistant to transmission (1 clone) when co-cultured with lymphoid cells. Furthermore, preliminary analysis of the virus derived from the mutants indicate unusually low levels of viral RNA. These data hint that the mutants are defective in their ability to recognise and efficiently package viral RNA. In order to unequivocally define the status of our candidate 'packaging mutants' we have constructed a series of cell lines which stably express high levels of of mutant virus. A detailed analysis of these cell lines will be presented.

WP.21 Comparative Sensitivity of Tests for Detection of HIV Infected Cells.

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HIV infectivity assays such as virus neutralization determinations require that sensitive methods be used for detection of infected cells so that infection can be detected as early as possible. We have developed two sensitive tests for detection of infected cells, an immunocytochemical slide test using APAAP methods (alkaline phosphatase anti alkaline phosphatase) and an ELISA p24 capture assay. These two tests were compared for sensitivity with two other methods for detecting infected cells, reverse transcriptase (RT) assays and hybridization of ^{32}P labeled core protein DNA probes with disrupted cells. The test samples were cultures of HTLV-IIIB infected H9 cells which had been serially diluted with H9 cells so that the cultures all contained 10^6 cells/ml but various concentrations of infected cells. The cells were washed prior to being serially diluted and were then cultured for 14 hours before being tested.

The lowest concentration of infected cells which the various tests could detect were as follows: the APAAP slide test, 0.01%; the capture test, 0.02% on pelleted cells and 0.2% on supernatant; the DNA probe hybridization test, 0.15%; the RT assay, 1.5%. The APAAP slide test and the capture assay were also comparable with each other when used over a two week period to detect emergence of infected cells in cultures of peripheral blood lymphocytes which had been infected with three serial 10-fold dilutions of HTLV-IIIB.

Since the capture assay is considerably less labor-intensive than the APAAP slide test but has comparable sensitivity, the capture assay is the better method for many types of infectivity assays. The APAAP slide test, however, has proven to be very effective for detecting HIV antigen presence in sections of tissues such as brain and lymph nodes.

WP.22 Use of Hapten Labeled DNA Probes for the Detection of HIV Sequences in Infected Cells. M. MANAK, G. KELLER, C. CUMMING, M. BOCKELMAN AND B. SISSON. Biotech Research Laboratories, Inc., Rockville, MD.

A hapten labeled DNA probe has been developed for the detection of HIV RNA in infected cells. A part of the HIV genome which includes sequences coding for the gag region of the virus were subcloned into a pBR322 vector, and the purified plasmid DNA was chemically labeled with dinitrobenzene. This probe was used to detect HIV sequences in infected H9 cells. Serial dilutions of infected cells were mixed with uninfected cells, and the RNA from a total of 10^6 cells was extracted with phenol and ethanol precipitated. The RNA was slot blotted onto nitrocellulose membranes using the slot blot apparatus of Schleicher and Schuell. The filters were baked and hybridized with the hapten labeled probe. Specific hybridization was visualized by reactivity with rabbit anti-hapten antibody followed by an alkaline phosphatase conjugated goat anti-rabbit IgG, and color development. The sensitivity of detection is 1 pg as tested on dilutions of plasmid DNA and was similar to that observed with a ^{32}P labeled probe and autoradiography. Virus nucleic acid sequences can be detected in extracts of as little as 10^4 infected cells (10^6 viral genome equivalents). For even greater sensitivity, the probe can be used to detect viral sequences in individual infected cells by in situ hybridization. Cells were fixed on microscope slides with 4% Paraformaldehyde and stored in 70% ethanol until tested. Following a 3 hour hybridization, infected cells were visualized by the double antibody system described above. Using this method, individual infected cells can be detected in a vast excess of uninfected cells.

WP.23 Incidence of Seronegativity to HIV and HTLV-I in individuals infected with either virus.

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One thousand AIDS/ARC patients and 120 adult T-cell leukemia or HTLV-I carriers were prospectively tested for antibodies to HIV or HTLV-I, respectively in an ELISA assay. One of 1000 AIDS/ARC patients (0.1%) were seronegative for anti-HIV antibodies and 1 of 120 HTLV-I infected patients (0.8%) were seronegative for anti-HTLV-I antibodies. Seronegativity was confirmed by Western blot and radioimmunoprecipitation assays and was repeatedly negative in several samples obtained over one year's time. HIV or HTLV-I infection was confirmed by detection of viral proteins by immunoperoxidase staining of infected tissue with antiviral monoclonal antibodies and by detection of viral nucleic acids via enzmatic amplification and oligomer restriction detection techniques. Hence, seronegativity to these 2 viruses occurs with a finite, but real, frequency. Enzymatic in vitro gene amplification identified both seronegative individuals and represents a sensitive and specific method to confirm the diagnosis of HIV and HTLV-I infection.

WP.24 Genetic Characterization of Biologically Different HIV-Variants

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Human immunodeficiency virus (HIV) was cultured from either peripheral blood lymphocytes (PBL) or in some cases from cerebrospinal fluid (CSF). Cultures for virus isolation were performed from more than 180 geman AIDS, ARC, LAS and virus exposed asymptomatic patients. These isolates differed remarkably in their biological properties (cytopathic effect on lymphocytes and replication rate).

In the majority of AIDS-patient with neurological symptoms well-growing strains were obtained from PBL, whereas all but 2 isolates from CSF of the same patients grew slow and to only low titres on PBL.

One isolate from PBL was molecularyly cloned. Restriction analysis and nucleotide sequencing of several of the clones revealed the simultaneous existence of at least 4 distinct HIV variants in the peripheral blood of the patient. The amino acid sequence divergence of the variants from LAV/HTLV III_B in the env/lor region was about 10% with multiple insertions and deletions.

While the isolate from the patient's periphery grew readyly and with the formation of big syncytia on PBL, the virus from his CSF grew badly and with only marginal CPE. The genetic characterization of this slowly growing strain is in progress.

WP.25 Localization of the Transmembrane Anchor Domain of the Envelope Glycoprotein, gp160, of Human Immunodeficiency Virus

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In order to understand the mechanism of HIV-1 infection, it is important to determine which domains of the HIV envelope glycoprotein are exposed on the surface of the virus. While there is general agreement that gp41 is an integral membrane protein, its orientation in the membrane, and the number of times it spans the viral envelope have yet to be determined. Hydropathic analysis of gp160 revealed two potential transmembrane biding domains, both occurring in gp41 (residues 512-541, and residues 684-707). We have attempted to identify the membrane anchor region by construction of a series of mutant gp160 genes with truncations or deletions occurring in the gp41 region. Transfection of thee variants into mammalian cells demonstrated that mutations that preserved the first hydrophobic domain in gp41 and deleted the second hydrophobic domain encoded proteins that were secreted from the cells.. These results demonstrate that the first hydrophobic domain of gp41 is not sufficient for membrane biding and suggest that the carboxyterminal 174 amino acids of gp160 contains the membrane anchor sequence. Although it is possible that the two hydrophobic domains in gp41 interact to form a membrane binding domain, the simplest model would suggest that the entire gp160 molecule, with the exception of the last 174 residues is exposed on the viral surface.

WP.26 Serodiagnosis of HIV-1-infections by an Oligopeptide ELISA

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The ELISA has been proven as a highly sensitive and specific method in HIV-diagnosis. Nevertheless, unspecific reactions resulting in false positive results occur due to impurities of the antigen preparations. This problem can be solved in principle by using defined synthetic oligopeptides representing well conserved epitopes from different structural proteins of HIV-1. A number of synthetic oligopeptides (synthesized by Dr.Frenzel, Biochrom) have been screened in different ELISAs for reactivity against HIV-positive sera or negative controls (blood donors or patients from routine virus-diagnostic). Four oligopeptides containing 21 aminoacids each representing different epitopes from the proteins p18, p24, gp41 or gp120 with an optimal serologic specifity were selected and combined as a mixture in an ELISA. It could be demonstrated that with SDS blot-confirmed HIV-positive sera a reactivity of 100 % could be obtained. 2729 out of 2735 negative sera were in this ELISA non-reactive, indicating a specificity of 99,8 %. The good specificity and sensitivity was underlined by a significant difference between the extinctions of the non-reactives and the reactives in so far as 97 % of the positive probes showed an extinction of > 1.95 and 99,3 % of the negatives an extinction of < 0.15.

WP.27 HIV antigenemia in patients with AIDS or related disorders : a study in European and Central African populations.

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The presence of human immunodeficiency virus antigen (s) (HIV-Ag) was analysed in the serum of AIDS patients, ARC patients and symptomless seropositive people using a solid-phase sandwich-type ELISA (Abbott, Abbott Park, Il.). Individuals entering the study were either French (group I) - or Central African residents (group 2).

GROUP I (Nb : 80) HIV Ag was detected in 48 % (10/21) of AIDS patients, 22 % (5/23) of ARC patients, and 3 % (1/36) of symptomless seropositive individuals. HIV antigenemia was correlated with the absence of antibody to HIV gag antigens with a competitive antibody immunoassay employing HIV core antigens produced by recombinant DNA technology (ENVACORE^R, Abbott). Fifteen out of 27 anti-gag negative individuals (56 %) were HIV-Ag positive against only 1 out of 53 anti-gag positive individuals (2 % ; $p<10^{-7}$). Longitudinal studies showed that HIV-Ag was transient in primary HIV infection. On the contrary, late appearence of HIV-Ag in seropositive individuals was associated with persistent antigenemia and seemed to correlate with clinical deterioration.

GROUP 2 (Nb : 144) Only 1 out of 55 AIDS patients (2 %) was HIV Ag positive. None of 52 ARC patients and 37 symptomless seropositive individuals presented HIV antigenemia. In contrast with European AIDS patients, 95 % of AIDS patients (55/58) from Central Africa were positive for antibody to HIV core antigens.

This study shows that expression of HIV-Ag in serum is correlated with absence or disappearance of antibody to gag antigens.

The clinical value of HIV antigenemia that may exist for seropositive European individuals cannot be applied to Central African seropositive populations. This observation has practical and fundamental implications that will be discussed.

WP.28 Expression of a Functional HIV tat-III Protein from a Chemically Synthesized Gene.

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The predicted 261 base pair coding sequence of HIV-IIIB tat-III has been chemically synthesized, cloned in E. coli and expressed in HeLa cells. The tat-III sequence was fused to a translational start signal and placed under SV40 early transcriptional control. Co-transfection of the synthetic tat-III gene along with a reporter gene (chloramphenicol acetyl tranferase or β-galactosidase) linked to an HIV LTR confirmed that the synthetic gene product exhibits similar activity to tat-III expressed from HIV genomic DNA in the trans-activation of the LTR. In the design of the synthetic coding sequence, unique restriction sites that do not change the primary amino acid sequence were introduced to facilitate assembly of the gene. These restriction sites can be used to easily replace segments of the gene with synthetic oligonucleotides containing any desired sequence changes (cassette mutagenesis). This approach is being used to analyze structural changes and their effect on the function of the tat-III gene product.

WP.29 Neurological AIDS: Isolation and characterization of noncytocidal natural variants of human immunodeficiency virus (HIV) from AIDS patients with neurological disorders

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Heterogeneity in AIDS virus isolates has been well documented but has not been correlated with the clinical manifestations of AIDS or with the functional biology of the virus. The occurence of central nervous system involvement in certain AIDS patients with minimal neurohistopathology prompted us to isolate viruses from such patients and delineate their cytopathic properties. Five virus isolates, termed NA1-NA5, were obtained from four neuro-AIDS (NA) patients. The isolates were identified as HIV by antigenic cross-reactivity and nucleic acid hybridization to HIV-specific antibodies and DNA probes. The replication and cytopathic properties of these isolates were studied and compared with lymphadenopathy-associated virus (LAV) in vitro. All NA isolates exhibited replication efficiency equivalent to LAV, but four of five isolates did not kill T4 cells. The frequency of T4-positive cells in LAV-infected cultures (normal adult peripheral blood lymphocytes) decreased to 1.6% in 15 days, but the frequency of T4-positive cells in uninfected cultures and in cultures infected with noncytocidal variants remained between 46% and 64%. These findings provide evidence for the existence of noncytocidal natural variants of HIV, and raise the possibility that in some AIDS patients neurologic disorders might be caused by HIV variants that are noncytocidal to T4 cells.

WP.30 A simple and economical HTLV-III TEST for underdevelop countries.

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Present HTLV-III tests require the use of equipment and technical skills not readily available in underdeveloped countries. In addition the cost per test make it impossible for these countries to establish a policy of individual testing for all blood donors. This has resulted in the practice of blood pooling in order to reduce cost.To overcome these problems,PASSIVE HEMAGGLUTINATION TEST (PHT) has been established.This test involve the fixed red cells sesitized with HTLV-III antigen. 25ul of sera samples of each do - nor is mixed in 25ul of phosphate buffer saline .15M pH 7.2 and adding 25ul of sensitized red cells.After 15min PHT become positive if agglutination patterns can be seen,and negative when cells do not agglutinate and form a well defined button.The specificity and sensitivity is exactly the same compared with ELISA.In regarding to reproductivity and stability is far better then ELISA when it was compared with 1000 sera samples of blood donnors,suspected and AIDS cases.All positive samples in any methods were confirmed by WESTERN BLOT.In conclusion the PHT is very easy to be done, to be read does not require the use of equipment or a trained technician·,and it is very fast;15min compared to 120min.The cost is only 1/20 of current methods,before adding the cost of equipment.

WP.31 Transmission of Human Immunodeficiency Virus to Non-hematopoietic Cells by Co-cultivation.

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Infection with human immunodeficiency virus (HIV) often induces neurological disorders. We examined susceptibilities of non-hematopoietic cell lines to HIV. HIV produced by H9/HTLV-III_B cells, kindly supplied by Dr. R. C. Gallo, was mainly used. NP-1, NP-2, U-251 MG and HOS human cells and S^+L^-CCC cat cells were co-cultivated with lethally irradiated HIV-producing Molt-4 cells. The former three cell lines had been derived from human gliomas. Only NP-1 cells (0.2-0.5%) became immunofluorescent on indirect immunofluorescence assay. Sera of seropositive hemophiliacs inhibited the transmission. U-251 MG cells were not susceptible to HIV, although these cells expressed glial fibrillary acidic protein which is known to be specifically detected in glial cells. On the other hand, 1-43% of NP-1, NP-2, U-251 MG, HOS or S^+L^-CCC cells became immunofluorescent after co-cultivation with T cells doubly infected with HTLV-1 and HIV. Thus, HIV was transmitted efficiently to non-hematopoietic cells in the presence of HTLV-1. Sera from ATL patients inhibited the transmission. HIV antigen-positive NP-1 and NP-2 cells were cloned. Each clone contained 1 or 2 copies of HIV genomes. Some clone produced infectious HIV abundantly, while some clone produced non-infectious HIV. Some clone contained defective HIV. The procedures described here may be useful for elucidation of biological and pathogenic properties of HIV.

WP.32 HIV-related viruses in pregnant women in Gabon.

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During a study of vertical transmission of retroviruses in Gabon (Nov.'85 to Nov.'86), serum samples from 750 women were collected each 3 months during and after pregnancy. Twenty-four sera were found HIV-1 positive by Elisa (Elavia). By HIV-1 Western blot (WB)(LAV-Blot), one serum was negative and 2 were confirmed as HIV-1 positive. Twenty-one sera did not fit the criteria for HIV-1 positivity but exhibited the p25 band associated to the p55 or to another band of about 37 kD (14 cases). The same banding pattern was found in all serial samples from each woman. All these 21 sera were HIV-1 negative by RIPA. By LAV-2/HIV-2 Elisa all 21 sera were negative and by HIV-2 WB all presented the p26, with no antibodies to the envelope glycoproteins.

We performed retrovirus isolation from peripheral blood lymphocytes from 2 of these 21 women. In the two cultures a reverse transcriptase activity (RTa)was detected at day 21 in the cell-free supernatants. The RTa persisted at the same level ($50x10^3$ - $90x10^3$ cpm/ml), without peak and with no obvious cytopathic effect on the infected T-lymphocytes. No decline of the lymphocyte proliferation was observed. The cell-free supernatants reacted with HIV-1 polyclonal antibody by an antigen capture assay. By an indirect IF assay the cultured infected T-lymphocytes from the 2 women reacted obviously with the sera of each patient and weakly with human HIV-1 antibodies. No reaction was observed with HTLV-I nor HIV-2 antibodies. Southern Blot analysis showed a weak hybridization with the entire HIV-1 genome in conditions of high stringency. In January 1987, all these women were healthy and their total lymphocytes count was normal.

WP.33 HIV Neutralizing Antibodies to a Recombinant Segment of the Virus Envelope: Studies with Multiple Virus Variants and Neutralizing Epitope Definition

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PBl, an E. coli produced segment from the carboxyl-terminal half of the gpl20 envelope protein, elicits antibodies that neutralize HIV infection in vitro (Science, 234, 1392-1395, (1986)). This neutralization is HIV strain specific. We have produced the same region from four other HIV isolates and used these as immunogens individually and in combinations to determine the virus neutralization patterns and to achieve an immunogen capable of eliciting broadly neutralizing antibodies. In addition, we have obtained fragments of PBl by genetic and proteolytic means to define more precisely the epitope that elicits the neutralizing response. These have been used as immunogens and in competition binding experiments with neutralizing sera. Implications of the results of these approaches for the development of an effective vaccine against AIDS will be discussed.

WP.34 Molecular Characterization of the Type D Retroviruses in Macaques

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A series of related, but genetically distinct type D retroviruses has been isolated from Asian macaques suffering from simian AIDS (SAIDS). Two serotypic groups are recognized: SRV I, originally isolated from the California and New England PRCs and most closely related to Mason-Pfizer monkey virus; and SRV II, isolated from the Oregon and Washington RPRCs and associated with the Kaposi's sarcoma-like neoplasm, retroperitoneal fibromatosis (RF). The SRV II strain (IIC) isolated from M. nigra with a high incidence of SAIDS/RF at the ORPRC has been cloned in collaboration with the CAPRC, and used to screen other macaque species at the ORPRC. Currently 5% of the rhesus colony (M. mulatta) are virus-infected, and an additional 25% have evidence of prior infection. The rhesus isolate (SRV IIR) is serologically indistinguishable but genetically distinct from SRV IIC, and is associated with a lower mortality rate. A severe form of SAIDS has also been observed in the Japanese macaque (M. fuscata) troop at the ORPRC. Restriction maps of isolates from affected animals are identical to SRV IIR. In contrast to our experience with M. mulatta, SRV IIR infection appears to result in clinical SAIDS and death in a high percentage of M. fuscata. Two SRV IIR isolates, one from a Japanese and one from a rhesus macaque, exhibit a slightly altered restriction pattern. These two variants appear to be identical to one another.

Recently, two M. mulatta imported from the People's Republic of China have been shown to be actively infected with a new type D SRV more closely related to SRV I than to SRV II. Investigations are underway to determine whether this strain constitutes a third serotype.

WP.35 Expression and Analysis of HIV gP120 Analogues Secreted from Saccharamyces Cerevisiae

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Yeast cells have been engineered to produce a secreted form of the HIV envelope glycoprotein (gP120). The 500 amino-acid coding region of the gP120 envelope gene was fused to the human serum albumin signal sequence and programmed for expression with the yeast chelatin promoter. The resulting plasmid was transformed into a wild type yeast strain (20B-12) or into a yeast mnn9 manno protein mutant (Tsai et al., J.B.C., 259, p. 3805, 1984). Proteins secreted from cells in the presence of copper were analyzed by immunoblotting and shown to react with several HIV gP120-positive human and rabbit sera. Secreted protein from wild type 20B-12 cells migrated as a >300 kd polypeptide smear on low percentage gels presumably due to hyperglycosylation of the envelope protein. However, protein from the supernatant of mnn9 cells migrated as a diffuse band at ~130 kd. In both cell lines, the secreted envelope glycoproteins were sensitive to N-glycanase treatment; however, only the 130 kd mnn9 protein bound to an immunoaffinity column containing human anti-HIV IgG. Rabbit sera directed against purified mnn9-gP130 reacted with native gP120 from HIV infected cells.

WP.36 Identification of gag-epitopes by a panel of MAb in a serie of HIV isolates

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Immunization of Balb/c mice with TX-100 disrupted sucrose gradient purified HIV enabled a panel of 10 monoclonals against HIV-gag products to be produced. Characterization by immunoblotting and radioimmunoprecipitation assay using ^{125}I-labeled HIV-proteins together identified 8 hybridomas which were reacting variously with gag-proteins pr55 and p24 and 2 hybridomas reacting with pr55 and p18. In order to characterize the different anti-gag clones a cross-competition RIA was developed. Purified IgG from each of the clones was labeled with ^{125}I and each clone allowed to compete with itself and all other clones as radiolabels for HIV antigens bound to sepharose beads. It was concluded that these monoclonals react with presumably 6 different gag-epitopes. Three of these were mapped on tryptic peptides. Different combinations of antibodies were used to detect the presence of HIV-gag products in various isolates by a p24 capture assay. CLB-21 as catching antibody and ^{125}I-CLB-14 as tagging antibody appeared to be the most broadly reactive of all antibodies. Screening of 70 HIV isolates positive in this capture assay, two isolates failed to react with CLB-47. This was not due to a low level of HIV expression since elevated levels of RT activity were observed. To explain this lack of reactivity, a genetic variation or post-translational modification of the anti-gag epitope might have occurred.

WP.37 Molecular Cloning and Nucleotide Sequence of a Highly Cytopathic Strain of Human Immunodeficiency Virus.

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A highly cytopathic variant of the human immunodeficiency virus type 1/ HIV1/ was isolated from a zaïrian patient with AIDS. When biologically tested on MT4 cells, a striking cytopathic effect, estimated to surpass at least one thousand times that of HIV 1 prototype was disclosed. Preliminary experiments suggested that this variant possesses a completely different restriction enzyme pattern in Southern blot analysis. In order to determine the putative genomic regions involved in observed biological features, a molecular cloning of this isolate proviral genome was accomplished. The genomic library was prepared from partially digested DNA of persistently infected CEM cell line and established by means of EMBL 3 vector. Recombinants were obtained on successive screening employing HIV 1 probes. The nucleotide sequence and resulting implications which will be presented might inform on the cytopathogenicity of AIDS viruses.

WP.38 Reactivation of Human Immunodeficiency Virus Long Terminal Repeats by Herpesvirus Infection

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We have shown recently that the expression of chloramphenicol acetyltransferase (CAT) directed by human immunodeficiency virus (HIV) long terminal repeat (LTR) in stably transfected cell lines can be activated both by HSV-I infection (Mosca, et al., Nature 325:67-70, 1987) and 5-azacytidine treatment (Bednarik, et al., J. Virol., In Press). Both HSV infection and 5-azacytidine treatment led to an increase in CAT activity, accumulation of CAT mRNA and an increase in CAT gene transcription, suggesting that the activation occurs at the transcriptional level. The HSV gene product responsible for HIV LTR activation was identified using HSV-1 ts mutants and the cloned HSV-I immediate-early genes for IE175K, IE110K proteins and the late structural protein Vmw65. The inducible region within the HIV LTR was identified using the Bal 31 deletions in the 5' region of HIV LTR. When a 71 nucleotide long fragment from HIV LTR was placed in front of a heterologous, non-inducible gene (murine α-39/+22 CAT), the expression of α-CAT gene was induced by HSV infection. The HIV LTR can also be induced by cytomegalovirus (CMV) infection; however, the results suggest that the activation by CMV does not occur through the same sequences that are recognized by the HSV factors. In addition to HSV-I induced activation, the effect of the HIV coded transactivation TAT protein on the HIV LTR was also investigated.

WP.39 Expression of Envelope Glycoproteins of Human Immunodeficiency Virus by an Insect Virus Vector

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The envelope gene of human immunodeficiency virus (HIV) has been inserted into the genome of an insect virus vector (Autographa californica nuclear polyhedrosis virus). Upon infection of tissue culture cells, this recombinant virus produced a 150k immunoreactive polypeptide related to the precursor envelope glycoprotein (gp150) of HIV. Radioisotope labeling with ^{3}H-mannose indicated that this recombinant-made polypeptide was glycosylated. Forty-eight hours after infection, immunoreactive proteins of molecular weights 120-130k and 41k were also detected. By their reactivity to monoclonal antibodies, these proteins were identified as analogs of mature envelope glycoproteins gp110 and gp41, respectively. To demonstrate the potential usefulness of these recombinant-made proteins in diagnostic tests for AIDS, we used infected cell lysates as antigens in a solid-phase immunoassay to screen a panel of 48 human sera. Results of this immunoassay correctly identified all positive and negative samples previously classified by Western blot and immunoassays based on disrupted virions. A relatively low cutoff value (OD=0.18) and a high signal-to-background ratio (average >9) were obtained using crude infected cell lysate without prior purification. Studies are also in progress to determine the immunogenic properties of the envelope glycoprotein analogs produced by insect virus vectors.

WP.40 Heterosexual Transmission Study in Infected Intravenous Drug Abusers

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In a cohort study of 250 intravenous drug abusers (IVDA) with a high seroprevalence of antibody to HIV (51% of 164 tested since September 1983) 14 couples were identified in which sexual relationship data were available to allow heterosexual transmission studies.

Stored serum (for hepatitis testing) allowed accurate identification of seroconversion dates and questionnaire data and the high evidence of pregnancy (6) confirmed the absence of barrier contraception during the study period.

The study group therefore was of 11 (92%) male and 1 (8%) female seropositives. When tested 2 (16%) of the female partners were found positive and the single male exposed sexually to HIV was negative.

The average length of exposure to HIV was 19.1 months in the whole group (19.2 in the non-converters and 18.5 months in those found to have transmitted the infection).

If the negative status indeed indicates non infection then it seems likely that transmission may not now take place.

The couples who had transmitted the virus were all positive at first testing and subsequent testing in the remaining couples has revealed no new seroconversions even in the continued absence of appropriate barrier contraception in most cases.

The problem of early transmission followed by apparent reduced infectiousness is similar to that seen amongst those continuing to share infected needles and syringes in Edinburgh.

WP.41 HIV Seroconversion In Intravenous Drug Abusers: Rate and Risk Factors

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We are studying the rate of and risk factors associated with HIV seroconversion in intravenous drug abusers attending a NYC methadone program. From July 1985-April 1986 subjects were enrolled in a prospective study of the natural history of HIV infection. Standardized interviews eliciting demographic data, drug use, sexual and medical histories and physical examinations were performed. Blood for serum antibodies to HIV was obtained.

Among 498 enrolled initially, 329 (66%) were seronegative (SN) and 169 (34%) seropositive (SP). During 16 mos. of follow-up, 142 (98 SN and 44 SP)had repeat HIV antibody determination. Nineteen of 98 original SN (19%) acquired HIV antibody after a mean 11 mos. of follow-up (range 4-16 mos.).

Interview data for the follow-up period are available for 128/142 (90%) of retested subjects, (92 SN, 36 SP). In this subgroup, 77 of 92 original SNs(84%) remained SN and 15 of 92 (16%) developed HIV antibody. All 36 SPs remained SP. Among demographic variables, non-white race, but not age or gender, was associated with seroconversion. Non-whites comprised 13/15 (87%) of seroconverters and 33/77 (43%) SNs ($p<.01$). Of the drug variables, seroconversion was associated with reported intravenous drug use during the follow-up period ($p<.01$), mean number of days per month using IV drugs ($p<.01$), use of "speedball" (heroin and cocaine mixed) ($p<.03$), but not heroin or cocaine alone. Of those injecting drugs, 11/15 (73%) of seroconverters reported sharing needles vs. 22/36 (61%) of SNs ($p>.05$). History of sex with another intravenous drug abuser was associated with seroconversion ($p<.01$). No seroconverters reported sex with prostitutes. Male homosexual activity was reported by one seroconverter and one SN only.

These preliminary data suggest that both intravenous drug use and sexual activity put heterosexual intravenous drug abusers at increased risk for HIV infection. SN intravenous drug abusers in a methadone program remain at high risk for development of HIV antibodies (19% at mean follow-up of 11 mos.) as long as high risk sexual and drug behavior continue.

WP.42 Seasonal Variation in AIDS and Opportunistic Diseases

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We looked for seasonal variation in the diagnosis of AIDS, and in the diagnosis of opportunistic diseases seen in AIDS patients. Seasonal variation in AIDS or in the initial opportunistic disease would suggest that an agent with a seasonal variation acts as a cofactor for the development of AIDS. Seasonal variation in subsequent opportunistic diseases could reflect the epidemiology of that disease in an already immunosuppressed population. We studied the number of diagnoses per month for U.S. AIDS cases during the 72 months from January 1980 through December 1985. The upward trend in diagnoses per month was adjusted for by linear regression, a von Hann filter was used to smooth the curve, and Roger's test for seasonality was applied. We observed small but statistically significant seasonality for the diagnosis of AIDS (12% difference, peak--summer, trough--winter, $p<0.00005$). For 9 initial manifestations of AIDS, we saw statistically significant seasonality only for Pneumocystis carinii pneumonia (14% difference, peak--summer, trough--winter, $p<0.005$) and Kaposi's sarcoma (15% difference, peak--summer, trough--winter, $p<0.005$). For 9 subsequent diagnoses, seasonal variation was seen only for cytomegalovirus infection (CMV) (34% difference, peak--spring, trough--fall, $p<0.05$). (Although not statistically significant, we noted a similar distribution for CMV as the initial manifestation of AIDS.) Primary lymphoma of the brain showed some seasonality both as the initial and as a subsequent diagnosis: when combined, this was a statistically significant difference (44% difference, peak--summer, trough--spring, $p<0.05$). We conclude that there is no important seasonality in the onset of AIDS, but there may be some seasonality to CMV and primary lymphoma of the brain in immunocompromised patients.

WP.43 Stability of HIV Infection Prevalence Over 10 Years in a Rural Population of Zaire.

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Five (0.8%) of 659 human serum specimens collected in the Equateur Province of Zaire in 1976 following an epidemic of Ebola hemorrhagic fever contained antibody to human immunodeficiency virus (HIV). Eighty-six previously seronegative persons were traced in 1985/1986 and were found to remain seronegative. A serosurvey in 1986 using a cluster sampling technique in the same communities showed a prevalence of HIV antibody of 0.8% in 389 healthy adult villagers sampled. In 136 pregnant women the seroprevalence rate was 2% and in 283 prostitutes 11%. Patients with AIDS were observed in hospitals in different parts of the Province. Their risk factors were increased numbers of sexual partners and residence outside of the area. HIV infection rates have not changed over 10 years and remain low in rural Equatorial Zaire, but risk groups have been identified. These findings suggest that social factors associated with urbanization are important in the rapid spread of AIDS in Africa.

WP.44 Field Assessment of an Enzyme Immunosorbent Assay for HIV Antigen (HIV Ag)

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Seven sites in N. America and Europe have assessed the reproducibility, sensitivity and specificity of solid phase enzyme immunosorbent assay (ELISA) to detect HIV Ag. Reproducibility was examined by multiple testing of 4 serial dilutions (89 to 968 pg/ml) of an HIV Ag positive specimen. The coefficient of variability ranged from 8-16% within and between run. The prevalence of HIV Ag and HIV antibodies, p24 and gp41, as markers of HIV infection was assessed in the following groups of individuals using specific ELISA's: 326 AIDS, 266 ARC, 436 seropositive asymptomatic subjects, 69 hemophiliacs, 274 seronegative asymptomatic subjects and control groups of 1460 healthy individuals and 345 patients with diseases other than AIDS. No HIV Ag or HIV antibodies to p24 and gp41 were detected in either control group or in seronegative asymptomatic individuals. Antibody to gp41 was a constant marker, present in 99 to 100% of seropositive specimens. The level of p24 antibody decreased with the severity of HIV symptoms from 81% in asymptomatic seropositives to 61% in ARC and 45% in AIDS patients. The prevalence of HIV Ag in seropositive subjects was 40% in AIOS, 24% in ARC and 7% in asymptomatic subjects. In summary, HIV infected individuals, demonstrate a direct correlation between increased antigenemia and the severity of symptoms. This may be predictive of the clinical complications of HIV infection, such as AIDS and ARC.

WP.45 Future Invasion of HIV into a Broader Spectrum of Americans Predicted from HBV Example.

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Hepatitis B virus (HBV) has transmission patterns remarkably similar to human immunodeficiency virus (HIV). As a result, the diseases caused by the two viruses occur in population subgroups whose behavior or medical therapies put them at risk of infection. HIV is a recently introduced virus which has yet to equilibrate in the American population. We have compared the results of transmission studies of HIV and HBV to judge the similarities of these viruses and the usefulness of HBV as a model to predict the future of HIV disease.

Overall, the transmission of HIV and HBV are remarkably similar. A side-by-side comparison of HBV and HIV in homosexual men found HIV to be about 1/4 as transmissible per exposure (Francis and Byers). Within this group the high carrier-to-infection ratio of HIV has more than made up for this discrepancy in terms of overall efficacy of spread. Prevalence and incidence studies of heterosexual groups exposed to infected male or female partners have shown essentially identical rates of infection for the two viruses. For IV drug users, it is clear that HIV can saturate the population in a manner very similar to HBV.

Because of the remarkable epidemiologic similarities of HIV and HBV, we presume that, if nothing is done to stop further extension of HIV infection, HIV disease patterns will eventually mirror HBV's. That will mean that about 1/2 the cases will have been infected through homosexual contact and/or IV drug use and 1/2 the cases will have been infected by either documented or presumed heterosexual exposure. The demography of cases, using the HBV prediction would change considerably. Whites would account for 67% of cases, blacks 24% and hispanics 8%; 67% would be male.

WP.46 Predictors of Survival for AIDS Cases in San Francisco.

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We evaluated survival following AIDS diagnosis for 2,489 patients reported in San Francisco between July, 1981 and September 30, 1986. Cases were followed at six month intervals from diagnosis to death. The maximum follow-up time was 70 months (mean = 17.8 months). Follow-up was nearly complete, with only 2 percent of cases known to be lost to follow-up. The median survival for all cases was 11.2 months, with a three year survival rate of 13.1 percent. Median survival varied significantly ($p<0.05$) with: initial diagnostic grouping (Kaposi's sarcoma = 17.3 months; Pneumocystis carinii pneumonia = 10.2 months; Both KS and PCP = 12.3 months; other opportunistic infections = 6.2 months); age at diagnosis ($\leq$ 19 yrs. = 3.2 months; 20-29 yrs. = 12.5 months; 30 - 39 yrs. = 12.0 months; 40 - 49 yrs. = 10.8 months; 50 - 59 yrs. = 8.2 months; $\geq$ 60 yrs. = 5.5 months): and risk group (homosexual/bisexual male = 11.2 months; IV drug user = 6.5 months; homosexual/bisexual IV drug user = 10.6 months; all other risk groups = 7.6 months. Median survival did not vary significantly with race, sex, or year of diagnosis. Cox proportional hazards regression analysis indicated that initial diagnostic group, and age at diagnosis were significant ($p<0.05$) predictors of survival in a multivariate model, while race, sex, risk category, and year of diagnosis were not. These data suggest that length of survival is primarily determined by initial diagnosis and age at diagnosis. Length of survival has not changed significantly since the beginning of the epidemic.

WP.47 Lymphadenopathy: Update of a 60 Month Prospective Study. DONALD I. ABRAMS, D.H. KIRN, D.W. FEIGAL AND P.A. VOLBERDING, San Francisco General Hospital, San Francisco, California USA

Two hundred homosexual men with persistent generalized lymphadenopathy (PGL) of greater than 6 months' duration involving two or more extrainguinal sites were enrolled in this natural history study initiated in November 1981. Current morbidity status information is available on 143 men. Of these, 47 (36%) have progressed to AIDS diagnoses. Twenty-seven patients developed Pneumocystis pneumonia, 16 Kaposi's sarcoma and 4 other opportunistic infections. The percentage of patients developing AIDS after 24 months of PGL by product limit estimates was 3.5% (± 1.5); 13% (±3.2) after 36 months; 32% (± 5.1) after 48 months and 45% (± 7.1) after 60 months. Significant factors predicting the development of AIDS include shrinking adenopathy; thrush or hairy leukoplakia; increased constitutional symptoms; peripheral cytopenias and an elevated erythrocyte sedimentation rate. Twenty-four of the AIDS cases died with a mean survival of 12 months. Five additional deaths occurred in cohort members who developed HIV-related non-AIDS diagnoses. A Kaplan-Meier analysis estimates an overall 5 year survival for patients with PGL of 73%. In view of the accelerating risk of developing AIDS appreciated from 36 months after the onset of PGL, participation in therapeutic intervention trials is warranted in this population.

WP.48 Epidemiology of AIDS and HIV-Infections in West-Germany

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Since 1982 voluntary reports on AIDS cases of West-German physicians to the Federal Health Office are evaluated. Five cases were reported in 1982, 39 in 1983, 90 in 1984, 243 in 1985 and 449 in 1986. Of the 860 cumulated cases (upto Jan. 1987) 50 appeared in females; death of 405 patients was reported; 77,5 % of the cases appeared in homo- or bisexual males, 6,4 % in hemophiliac, 6,1 % in i.v. drug abusers, 3 % in heterosexual partners of risk groups, 1,1 % in blood transfusion recipients, 1,3 % in children of HIVinfected mothers, in 3,8 % the risk factor is unknown. Of the female AIDS-patients 47 % were i.v. drug abusers, 29 % had HIV-infected sexpartners. The development of annual incidence rates and involvement of new risk groups in different geographical regions (e.g. major cities) are presented and compared to the preceding epidemiological situation in USA. Increasing numbers of reports on patients with neurological problems associated with AIDS (e.g. AIDS dementia complex) were recieved in 1986 (about 35 % of cases diagnosed in 1986).

Seroepidemiological data on HIV-infections in various risk groups and preliminary results of an ongoing multicentric screening study on prevalence of HIV-infections in pregnant woman and the underlying risk factors involved will be presented.

WP.49 Seasonal Trend in AIDS Case Numbers in Seattle-King County, Washington 1984-1986. SHARON HOPKINS, D. Bolgiano. Seattle-King County Department of Public Health. Seattle, Washington, USA.

Analysis of AIDS case numbers reported in King County residents by quarter-year of diagnosis for 1984-86 revealed a consistent pattern. The table below indicates proportion of cases per quarter by year. Quarter I is January, February, March, Quarter II is March, April, May, and so on.

	Quarter of Diagnosis				
	I	II	III	IV	
1984	.17	.25	.31	.27	Proportion
1985	.15	.28	.30	.27	of
1986	.20	.25	.35	.20	Cases

This seasonal variation may relate to patterns of care-seeking, changes in human activities by season, coveriebility of secondary pathogens, or environmental factors which may contribute to the development of AIDS in human immunodeficiency virus (HIV) infected persons. Recent studies suggest that intredermal Langerhans cells may serve as a reservoir of HIV and that an abnormality in their number or function may be involved in the pathogenesis of AIDS. As a result of their location in skin, Langerhens cells may be influenced by sunlight. Thus, we hypothesized a causal relationship may exsist between veriability in ambient sunlight and numbers of AIDS cases.

Analysis of local weather data supported the suspected relationship. When a log-linear model was fit to case numbers, the effect of minutes of sunlight per quarter-year was significant after adjusting for year of diagnosis. Our investigation should be considered preliminary, yet suggests directions for further research.

WP.50 Does prenatal human immnodeficiency virus (HIV) infection produce infant malformations?

JOANNE EMBREE, M BRADDICK, JO NDINYA-ACHOLA, B LOW, J MURITHII, C HOFF, et al. Univ Nairobi, Nairobi City Commission, Nairobi, Kenya; Univ Manitoba, Winnipeg; Univ S Alabama, Middlesex Hospital, Lodon, UK; Institute of Tropical Medicine, Antwerp, Belgium.

A dysmorphic syndrome consisting of growth failure, microcephaly, and craniofacial abnormalities has been described in children with AIDS born to drug abusing mothers. To evaluate the frequency of anomalies associated with congenital HIV infection in a non-drug abusing population. Newborns enrolled in a prospective study of perinatal transmission of HIV infection were assessed for the presence of 67 anomalous features. To date, 27 infants born to HIV seropositive mothers (by ELISA and western blot assays) and 19 infants of HIV seronegative mothers have been assessed. A single feature, a long philtrum, has been found more frequently in infants of HIV seropositive mothers (12/24 (46 %) vs 4/19 (21 %), p = 0.03). No difference in mean number of anomalies (2.3 vs 2.1) nor in percentage of infants with more than 3 anomalies (9/27 (33 %) vs 6/19 (31 %)) was seen between the two groups. Thus, no clear dysmorphic syndrome was found which would distinguish an infant born to an HIV seropositive mother.

WP.51 EVALUATION of an INDIRECT IMMUNOFLUORESCENCE ASSAY for HIV ANTIBODY DETECTION

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In collaboration with Organon teknika and indirect immunofluorescence assay kit (IFA1) for the detection of antibodies to HIV developed by IAF PRODUCTION INC was compared with an inhouse indirect immunofluorescence assay (IFA2) and an immunoblot assay (IBA). These tests were performed on 100 African and 95 European sera of which 58 % and 13.7 % respectively, were positive in IBA.

HIV infected H9 cells (H9) and non infected H9 were used as antigen and control antigen in the IFA1 and the ARV4 infected HUT78 cells and non infected HUT78 cells were used in IFA2. IFA results were read independently by three individuals. There was a concordance of 95.4 % between the two IFA test systems. The concordance with the IBA was respectively 93.3 % for IFA1 and 92.8 % for IFA2. The sensitivity for both IFA systems was 100 % when European sera were tested. IFA2 was less sensitive for the African sera (91.4 %). The specificity of the IFA's was slightly better for the African than for the European samples, respectively 95.2 % and 86.6 % for IFA1 and 100 % and 89 % for IFA2. No significant difference in titer was observed after parallel titration of several sera with the two methods.

We conclude that a commercially available IFA kit can be an inexpensive confirmatory test.

WP.52 Projections of Cumulative Case Frequency of Acquired Immunodeficiency Syndrome in the Bronx, New York: A Study in Small Area Analysis Comparing Two Different Models

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Minimum and maximum estimates of cumulative AIDS prevalence through 1991 were made for the Bronx, a borough of New York City with 1.16 million persons and a pattern of AIDS characteristic of areas with high rates of intravenous drug abuse (IVDA), e.g., 60% IVDA, 20% female, 89% Black and Latin, 4.5% children. Both models build on empirical data on reported AIDS cases. The first was developed by M. Morgan (CDC) and is a quadratic formula with conservative assumptions correcting for late reporting. As the proportion of Bronx AIDS cases to all U.S. cases has not varied significantly from 4.1% in each year from 1981 to 1986, national estimates based on the Morgan model were multiplied by 4.1% to estimate Bronx AIDS cases through 1991, correcting for late reporting of 1985 cases. The second model followed the method of A.D.J. Robertson, et al.: Nature, 1987 (in press), using a linear regression of logarithmically transformed prevalence data, and a 12 month doubling time empirically derived from the best fitting straight line from recent years. The CDC non-linear model yields a cumulative prevalence of 10900 cases of AIDS in the Bronx through 1991, while the linear model estimates 50600 cases. The cumulative AIDS prevalence rate in the Bronx would reach 990 cases/100000 persons to 4600/100000 by 1991 (1 per 101 persons to 1 per 22 persons). The implications for the public health of an epidemic of this magnitude in the Bronx community are discussed, particularly risk to sexual partners of infected persons, increased vertical transmission, and increased burden of AIDS-related illnesses.

WP.53 Human Immunodeficiency Virus (HIV) Infection Among Prostitutes in Nevada.

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None of 535 prostitutes in three legalized Nevada brothels were infected by HIV as compared to 23 of 370 prostitutes incarcerated in the State prison ($p<.001$). To evaluate the source of infection and sssociated risk we examined several factors.

Among the brothel sample, 7% shared needles during intravenous drug use over the last five years as compared to 100% of the inmates. 37% of the brothel sample were aware of contact with high risk partners (bisexuals or intravenous drug users), whereas 91% of the inmates reported contact with a high risk man (all intravenous drug users). Detailed sexual behavior was available for a 10% sample of the brothel prostitutes and for half of the seropositive women in the prison. The brothel prostitutes had more male partners over the last five years than the incarcerated women (median: 2191 and 20, respectively). All of the women engaged in vaginal intercourse; 30% of the brothel sample reported anal intercourse as compared to 44% of the incarcerated sample. None of the women in either sample reported consistent condom use by their sexual partners for any kind of sexual contact. We conclude that among prostitutes, needle sharing during intravenous drug use or sexual contact with a male intravenous drug user presents a greater risk for HIV transmission than the number of male sexual partners.

WP.54 Relationship between Recovery of HIV from Plasma and Stage of Disease.

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Previous studies have indicated that the lowest recovery of HIV from peripheral blood lymphocytes (PBL), but the highest frequency of detecting HIV p24 antigen in serum has been from patients with advanced HIV infection. To evaluate potential virologic markers for severity of HIV infections we cultured the PBLs and plasma of 72 patients with HIV infection: 9 CDC class II, 10 CDC class III, 53 CDC class IV patients, and 30 seronegative controls. PBLs were separated by density centrifugation. The plasma fraction was collected separately and filtered through a .45um filter. Plasma and PBLs were inoculated separately into PHA-stimulated lymphocyte cultures and assayed at weekly intervals for reverse transcriptase (RT). Cultures were done without knowledge of patient source. All 72 patients had HIV recovered from PBLs compared to 0 of 30 controls. HIV was recovered from the plasma in 22.2%, 28.6%, and 86.8% of CDC class II, III and IV patients, respectively. (P .01 between class II & III vs IV). The geometric mean cpm/ml of RT activity for the first and second postive culture supernatants were: plasma--CDC-II+III (29,391/552,515) and CDC-IV (144,465/522,257); PBLs--CDC-II+III (124,039/751,090) and CDC-IV (212,387/805,576). The percent of cultures that were RT positive by day 14 were 100% of CDC-II, 80% of CDC-III, and 94% of CDC-IV PBLs. For plasma these were 11%, 14%, and 68%, respectively. The frequency of isolating HIV from filtered plasma increases with advancing stage of disease. Studies correlating progression of HIV infection with presence and titer of HIV in plasma should be pursued.

WP.55 Elevated Urinary Excretion of Modified Nucleosides in HIV Positive Asymptomatic Women in a Methadone Maintenance Program

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Cancer patients and male subjects with AIDS or at risk for AIDS excrete in their urine increased amounts of modified purines and pyrimidines. Urinary modified nucleosides and 2-pyridone-5-carboxamide-N^1-ribofuranoside (PCNR) were measured from 110 former drug users. The subjects stopped using IV drugs between 1974 and 1985. HIV antibody was found in 46 (42%) of the volunteers. Modified nucleosides and PCNR were quantitated by HPLC and expressed relative to urinary creatinine. The asymptomatic women positive for HIV antibody excreted elevated levels of modified nucleosides and PCNR compared with the women who were negative for HIV antibody. The elevated modified nucleosides and PCNR are listed with their statistical significance analyzed by chi square: 1-methylinosine (0.0004); 1-methylguanosine (0.002); 1-methyladenosine (0.003); N^2_2-dimethylguanosine (0.0076); N^2-methylguanosine (0.017); pseudouridine (0.02); PCNR (0.089). The excretion of two nucleosides, N^4-acetyl cytidine and N^6-threonyladenosine was not elevated in the women positive for HIV antibody. These results are similar to homosexual men positive for HIV antibody. Relationship between drug use, other viral infections and the modified nucleosides will also be discussed.

Supported by New York State Department of Health and NIH HD20612.

WP.56 Proposed Revision of the AIDS Case Definition.

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The Centers for Disease Control (CDC) is coordinating a revision of the case definition of AIDS used for reporting in the United States. The objectives of the revision are 1) to track more effectively the most serious morbidity associated with human immunodeficiency virus (HIV) infection, 2) to simplify reporting of AIDS cases, 3) to increase the sensitivity and specificity of the case definition through greater application of HIV-antibody test results, and 4) to be consistent with current diagnostic practice. For patients with HIV antibody, the major proposed changes are 1) inclusion of HIV encephalopathy (dementia complex), HIV wasting syndrome, and a broader range of specific AIDS-indicative diseases, 2) inclusion as a separate category AIDS patients whose indicator diseases are diagnosed presumptively (who are not currently reportable), and 3) elimination of the requirement of absence of other causes of immunodeficiency. Suspected AIDS patients with a negative HIV antibody test would be excluded for surveillance purposes unless they had Pneumocystis carinii pneumonia or a T4 (T-helper) lymphocyte count <400/cubic mm. The proposed revision was developed in consultation with clinical specialists and local and state epidemiologists. Wide-scale implementation of the revised definition will depend on adoption at the 1987 meeting of the Conference of State and Territorial Epidemiologists. In the last quarter of 1986, about half of AIDS case reports included HIV-antibody test results, of which 97% were positive. The revised AIDS case definition should encourage greater diagnosti application of the HIV-antibody test. The effectiveness of the revision will, in turn, depend on how extensively the test is applied.

WP.57 Sexual and Other Practices and Risk of HIV Infection in a Cohort 450 Sexually Active Women in San Francisco.

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A prospective study of sexually active women at risk for HIV infection w begun in 1985 by the Association for Women's AIDS Research and Education (AWARE). At entry, all women met one or both of the following conditions: 1)at least one sexual relationship with a male partner known to be HIV infected and/or bisexual and/or an IV drug user; 2)multiple sexual relationships with male partners not in AIDS risk groups, or whose risk status is unknown. Participants included women working in the sex industry and women who used drugs intravenously. All women completed a detailed interview about their health, sexual partners and practices, and other AIDS risk-related activities since 1980. The overall prevalence of HIV seropositivity was 5%. Crude relative odds for HIV seropositivity were calculated for selected characteristics.

Over Last 3 Years	Relative Odds	p value
I.V. drug partner(s)	2.51	<.001
Bisexual partner(s)	1.45	.469
More than 10 partners	0.70	.761
Sex during menses	2.42	<.001
Any anal sex	1.14	.881
Anal sex without condom	1.28	.788
Self I.V. drug use	4.75	<.001

These findings indicate that a relationship with an I.V. drug using or bisexual male partner conveys more risk of acquisition of HIV than multiple partner exposure. The high risk observed with sex during menses warrants further investigation and analysis.

WP.58 Oral Candidiasis and Progression to Initial AIDS Associated Opportunistic Infection:

DAVID W. FEIGAL, D.I. ABRAMS, J.S. GREENSPAN, D. GREENSPAN, P.A. VOLBERDING, H. HOLLANDER, J. ZIEGLER, M.A. CONANT, University of California, San Francisco, CA, USA.

A clinical cohort of 1396 patients (pts) at the out-patient AIDS clinics of the teaching hospitals at the University of California, San Francisco, has been prospectively examined since Jan 1985. At entry, 297 study participants had Kaposi's sarcoma (KS), 402 Pneumocystis carinii Pneumonia, 75 both, and the remeinder ARC. Since dates of AIDS related opportunistic infections and oral candidiasis are recorded the progression from oral candidiasis, as one of the components of ARC, to AIDS can be estimated.

312 pts reported their first episode of oral candidiasis before any AIDS associated opportunistic infection (OI) or KS. 43% also had constitutional symptoms (BSx)· night sweats, 35% fever, and 22% wt loss greater than 10 lbs. Progression to an AIDS OI was estimated by the Kaplan-Meier method· 1 month 9% (+2%), 2 months 13% (+2%), 3 months 19% (+2%), 6 months 30% (+13%), 9 months 35% (+3%), 1 year 43% (+4%), and 18 months 48% (+4%). BSx when considered simultaneously with candidiasis did not significantly change the progression times.

Candidiasis on physical examination was a common finding in cohort participants, seen on 23% of initial examinations. Given the short time to progression for a significant proportion of pts, this is a clinical population that potentially demonstrate benefits of antiviral or immune modulating agents, while at an earlier stage of HIV infection.

WP.59 DISEASE OUTCOME AMONG HETERDSEXUAL AFRICANS WITH HIV INFECTION.

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During a 4-year period we surveyed in Brussels 102 HIV seropositive Central African patients (P) identified by ELISA and Western blot techniques. There were 49 males (mean age: 37y.) and 53 females (mean age: 28y.). None of the P recognized homosexual practice nor IV drug use. 9 (9%) had a previous history of blood transfusion during the last 10y. All people were examined at at least a 3mo period during a mean of 16mo. According to their clinical and immunological status, they were classified as healthy asymptomatic (stage I) (n=7), lymphadenopathy (stage II) (n=36), AIDS-Related complex (stage III) (n=38) and AIDS (stage IV) (n=21). During the study period no healthy seropositive developed signs or symptoms of HIV infection. 3 out of 36 P (8.3%) at stage II developed AIDS after a mean evolution of 33mo (range: 23-41) (annual rate of progression to AIDS of 1.1%). 12 out of 38 P at stage III (32%) developed AIDS at a mean time of 7mo (range: 1-23) (annual rate of progression of 20.7%). 21/36 P with AIDS died after a mean evolution of 5mo (range: 1 to 7mo).

These rates of progression to AIDS suggest that the natural history of HIV infection among heterosexual African patients is similar to that of American or European male homosexuals or bisexuals.

WP.60 WOMEN WITH AIDS/ARC: A CONTINUING STUDY

ADRIANA GRIGORIU, M.D., PATRICIA KLOSER, M.D., RAJENDRA KAPILA, M.D. University of Medicine and Dentistry, Newark, N.J. U.S

One hundred eighty five women seen at UMDNJ between December1980 and December,1986 have met recent CDC criteria Group II through Group IV. Greater than 90% of this patients are black with a history of parenteral drug abuse and/or sexual contact with parenteral drug abuser(s). The opportunistic infections of greatest prevalence continued to be PCP 50%, TB 30%, cryptococcal meningitis 20% and toxoplasmosis 2.5% with almost universal incidence of oral candidiasis and lymphadenopathy at some time during the illness.

The sexual life style of our patients is heterosexual with a small minority of bisexual women. A majority of our patients had gynecological problems including multiple ovarian cysts 9%, PID 7% secondary amenorrhea 40%, herpes genitalis 10% and persistant vaginitis 25%. There were a total of 17 pregnancies with such complications as fetal wastage, early abortions, premature delivery and death. Maternal morbidity and mortality continues to be a major problem. In the five year period from December, 1980 through December, 1985 we reported our findings on 53 women. The 132 new women represent more than double the total number of the previous 5 year period.

The reported 185 women in this study represent 61% of the total women with AIDS in New Jersey and 9% of the total nationwide(as of January 1, 1987).

The rate of increase in the number of women with AIDS in Newark and natinwide represents a major medical and social concern.

WP.61 Surveillance for HIV-related disease that does not meet the CDC AIDS Case Definition: Upstate New York

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Through January 1, 1987, 1329 cases of "suspect" AIDS were reported to the New York State Department of Health from among residents of counties outside of New York City. Of these, 804 (60.5%) met the CDC surveillance definition of AIDS. Of the 525 non-confirmed cases, active surveillance has been completed for 317, of which 139 (44%) are seropositive (by ELISA and Western Blot) for HIV antibody. All were hospitalized at the time of the diagnosis suggestive of AIDS and 32 (23%) are dead. Twenty-seven (19%) were diagnosed with secondary infections and cancers suggestive of AIDS (Group IVC1 and IVD), while 12%, 3% and 12% belonged to Groups IVA, IVB and IVC2 of the CDC classification system respectively. Twenty-eight of the 29 in groups IVC and IVD were diagnosed by the inappropriate method.

Compared to the 115 confirmed AIDS cases known to be HIV seropositive in the Upstate registry, non-confirmed HIV seropositive cases were more likely to be female (22% vs. 15%) or Black (36% vs. 21%) or IV drug users (45% vs. 36%).

The data suggest that females, Blacks and IV drug users are over-represented among reported cases of HIV-related disease that do not meet the CDC case definition for AIDS. These findings support the perception that use of the strict CDC case-definition may distort the epidemiology of serious HIV-related disease, especially for some subgroups.

WP.62 Perinatal Transmission of the Human Immunodeficiency Virus: A Longitudinal Study of the Children

New York City Collaborative Study Group for Vertical Transmission of HIV, (ELAINE J. ABRAMS, Harlem Hospital Center, New York, N.Y. Presenter)

This collaborative study aims to examine the effects of the HIV virus on high risk women and their babies. Clinical, serologic and immunologic data are collected prospectively on high risk women through pregnancy and one year postpartum. The children are followed by the same parameters for two years. Of 43 babies enrolled to date, 17 are less than 2 months of age; 15 are 2-4 months; 11 are 6-9 months. 24 babies are HIV antibody positive, 16 are negative; 3 are pending. No appreciable difference was noted in risk factors (IV drug use, sexual partner, both) for positive and negative mothers. All antibody positive babies have positive mothers. All antibody negative babies have negative mothers. No babies seroconverted. No significant difference was noted in average birth weight for positive and negative babies $\geq$ 37 weeks gestation (positive - 2796±451, negative 3091±499, grams ± S.D.) Head circumference at birth was comparable for both groups. No notable difference was found in the rate of preterm and SGA births. Serologic studies including IgG, IgM, IgA and T cell subsets were not significantly different for positive and negative babies at birth. Seven babies with positive serology are greater than six months old. Three have developed AIDS-related complex. One child has diffuse lymphadenopathy, recurrent candidiasis and recurrent otitis. Two are well and one is lost to follow-up. One positive baby presented DOA at three months of age. No other positive babies have illnesses suggestive of HIV infection.

WP.63 NO HIV SEROCONVERSION AMONG MEN REFRAINING FROM ANAL-GENITAL INTERCOURSE

ROGER OETELS, B VISSCHER, L KINGSLEY, J CHMIEL, ET AL. Multicenter AIDS Cohort Study, NIAID, Bethesda, MD.

A cohort of 733 HIV antibody negative men in Los Angeles was followed for 18 months. HIV seroconversion demonstrated by the Genetic Systems and Dupont ELISA tests and confirmed by Western Blot was compared among participants stratified according to reported sexual activities in the previous six months. No seroconversions occurred among men refraining from anal-genital intercourse.

Receptive and insertive:	50/522 (9.6%)
Receptive, not insertive:	2/35 (5.7%)
Insertive, not receptive:	2/126 (1.6%)
No anal-genital intercourse:	0/50 (0%)

Over sixty percent of those refraining from anal-genital intercourse reported one or more sexual activities with exchange of fluids including 31% swallowing semen. Although seroconversion rates were higher for those practicing receptive but not insertive anal-genital intercourse than for vice-versa the insertive but not receptive group had an average of twice as many partners suggesting a lower level of transmission efficiency for insertive anal-genital intercourse. This latter finding is consistent with reports that vaginal transmission from female to male does occur, but at an apparently low rate of efficiency. The demonstration of litte or no transmission from activities other than anal-genital intercourse over 18 months of follow-up provides a rational basis for prevention of infection through public health education. We are adding data for 24 months of follow-up from an additional 138 seroconverters in Baltimore, Chicago and Pittsburgh.

WP.64 MAINTAINING A STABLE LEVEL OF CD-4 CELLS IS A FAVORABLE PROGNOSTIC SIGN AMONG HIV POSITIVE MEN

JOHN FAHEY, R DETELS, B VISSCHER, A MUNOZ, A SAAH, V CLARK, ET AL. Multicenter AIDS Cohort Study, NIAID, Bethesda, MD.

A cohort of 537 HIV positive homosexual men in Los Angeles was followed for 18 months for changes in number of CD-4 cells. Seventy-one men subsequently developed AIDS. The mean slope of CD-4 cells among men developing AIDS was -.356/day (s.d. = .42) compared to -.01/day (s.d. = .01) among other seropositives. The distribution of slopes observed were:

	Slope of CD-4		
	< minus .17	-.17 to + .17	> plus .17
AIDS	70% (50)	20% (14)	10% (7)
Other Seropositives	27% (127)	48% (221)	25% (117)

The mean slope of CD-4 cells was downward among men developing AIDS whose initial levels of CD-4 cells were <200, 200-499 and >499 cells/mm^3 whereas the slopes among other seropositives demonstrated regression to the mean. The "flat" slope in men not developing AIDS suggests that CD-4 level may not he an appropriate surrogate for time since HIV infection. We did not follow these men from time of infection, therefore, some of those developing AIDS may have had a flat slope for some interval during the induction period. Nonetheless, these observations support the hypothesis that maintaining a stable level of CD-4 cells, even though it is at a lower level than seen among HIV negative men is a favorable prognostic sign over at least a period of 18 months. We will expand the data to include 1300 more HIV seropositive men from Baltimore, Chicago and Pittsburgh.

WP.65 *Are absence or progressive loss of antibody to individual viral proteins of HIV, predictors for development of AIDS? M. LANGE, K.R. ONG, E.B. KLEIN, K. SHRIVER, L. GOLDSTEIN, L.Z. COOPER, St. Luke's/ Roosevelt Hospital Center, Columbia University, New York, N.Y. and Genetic Systems, Seattle, Washington.*

A low level or complete disappearance of antibody to the human immunodeficiency virus has been reported by a number of investigators as a predictor of progression towards overt clinical AIDS. In order to evaluate whether this observation reflects a decreased antibody response to specific viral proteins, western blots (WB) and radioimmunoprecipitation assays (RIP) were performed on sera collected sequentially over a two year period from 10 AIDS patients and 26 HIV-pos subjects with or without lymphadenopathy (PGL) progressing towards overt AIDS and to ARC. Of patients with AIDS, 9 had no response to P55, 6 had no or weak (PW) response to p25 and 8 had an absent or PW to p15/17. Of 26 HIV-pos patients at time of entry, 11 remained asymomatic with or without Lymphadenopathy (PGL). Only one had absent Ab to P55 whereas others had a good AB response to all viral proteins. Of the 7 who progressed to overt AIDS most had an absent or progressively weaker AB response to P55 and P40 on western blot and an absent or weak response to P40 and P18 on RIP. This abnormal response was frequently present 1 year or more prior to the development of overt AIDS. Using regular ELISA testing, no correlation was detected between ELISA values and absence or presence of antibody to the above viral proteins. Although titration was not attempted, one may assume that antibody for specific viral proteins may be precipitated in circulating immune complexes frequently found in AIDS or ARC. In favor of this Hypothesis are our previously reported findings of presence of HIV antibody in CIC purified from sera of AIDS patients.

WP.66 Detection of Early HIV Seroconversion with Currently Available Serologic Techniques

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Early immune responses to products of env and gag genes of HIV have not been investigated extensively in large numbers of newly infected persons. Serial sera were collected from 45 seroconverters participating in the Baltimore center of the Multicenter AIDS Cohort Study. Seroconversion in this high risk group was defined as new and persistent appearance of antibody to p24/gp41/gp>100 on immunoblot, or of antibody to p24/gp120/gp160 by radioimmunoprecipitation assay (RIPA). We determined the sensitivity of seven EIA kits, two immunoblot kits and RIPA in detecting serologic markers of HIV infection at this early stage. The sensitivities of EIA kits were 76% to 92%; of the immunoblot kits, 82% to 96%; and of RIPA, 82%. Of interest, p24 antigen was detected in the serum of 4 of 45 seroconverters at a visit six months prior to the visit at which presence of anti-HIV antibody was confirmed.

Seven participants had baseline sera with serologic evidence of early HIV infection. The EIA kits were positive in 0-4 of the seven; RIPA was positive in 3/7; and one immunoblot kit failed to detect antibody in any of the seven.

We will discuss the probable sequence of serologic events in persons newly infected with HIV. These findings have important implications for the optimization of serologic tests for early HIV infection, especially for application in blood banks.

WP.67 Incidence and Significance of Persistent Generalized Lymphadenopathy in a Large Cohort of Gay/Bisexual Men

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Neither the incidence of new lymphadenopathy nor its place in the natural history of HIV infection is fully established. From 4 semiannual examinations during an 18-month interval, we have documented the incidence (Table) and examined the prognostic significance of persistent generalized lymphadenopathy (PGL) in HIV- men (Initial N=2635), seroconverters (Initial N=150), and HIV+ men (Initial N=1625).

	PGL at entry (%)	New PGL after entry: 0-6 mo(%)	7-12 mo(%)	Cumulative (12 mo)
HIV(-)	3	2	1	3
Seroconverters	11	23	14	33
HIV(+)	30	11	9	19

PGL was more common in men when their ELISA was last negative prior to seroconversion (11%) than in men whose negative ELISA remained unchanged for at least 6 months (3%)($p<0.001$); early viral response could be an explanation. Seroconverters developed PGL at 2x the rate seen in men who were HIV+ for an unknown length of time and 10x the rate seen in those who remained HIV-.

Prior to developing new PGL, previously HIV+ men closely resembled those without adenopathy in their mean CD4 and CD8 counts. During 12 months' follow-up, in neither HIV+ men nor seroconverters was the decline in CD4 count related to the presence of adenopathy, and PGL did not alter the risk of AIDS.

The incidence of PGL with new HIV infection is high, but its importance in the progression to serious immunodeficiency is not apparent.

WP.68 AIDS-Related Kaposi's Sarcoma in New York City in 1977

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New York City has been an epicenter of the AIDS epidemic since it was first reported in 1981, having both the earliest and the most cases of any city in the United States. We have shown that changes in the frequency of Kaposi's sarcoma (KS) cases among single young men are a sensitive means of detecting the AIDS epidemic. In this study, we reviewed the KS cases among young men <50 years old in New York City using data collected by the New York State Cancer Registry. Reliable data were available from 1973. Of 5 cases between 1973 and 1976 (1.25 cases per year), 4 were foreign born (including 1 from Puerto Rico), and were known to have been married. Four were also described as having disease of the the lower limbs compatible with classical, non-AIDS related KS.

In 1977, both the frequency and the demographic/clinical patterns of KS among young New York men changed. Of the 5 cases in that year, 3 were single men, all from the United States. In 1978, another single American-born cases occurred. In 1979, the recognized onset of the epidemic, 5 KS cases were reported, 4 of which were single. Of the 6 cases in 1980, 4 were single; and of the 31 cases in 1981, 28 were single. Clinically, 2 of the 6 cases in 1977/78 were recorded in unusual sites for classical KS, ear and penis; 3 were recorded as having KS of the "skin"; and only 1 was recorded as having disease limited to the limbs. Three of these 6 cases, all single, were from lower Manhattan, although none of the earlier cases were. These data suggest that the AIDS epidemic emerged in New York City in 1977.

WP.69 Association of Plasmids and Virulence of Mycobacterium avium Complex

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Organisms of Mycobacterium avium intracellulare complex (MAC) cause pulmonary disease in humans and frequently encountered as opportunistic pathogens in Acquired Immunodeficiency Syndrome (AIDS) patients. Our studies comparing the MAC strains of AIDS patients with those from non-AIDS patients showed a possible relationship with the presence of plasmids in the MAC strains. We have shown that 100% of 26 AIDS strains and only one-third of 150 non-AIDS strains possessed plasmids. To obtain specific and direct evidence on the relationship of virulence to plasmid content, blind comparisons were undertaken to assess the virulence and associated parameters of MAC strain LR-25 which was shown to possess three (2 small and 1 large) plasmids and a strain derived from it, designated as LR-163, which has been cured of the three plasmids by acriflavin treatment. Strain LR-25 consistently caused high mortality (45%) of beige mice and CFU counts of the organisms from spleens and lungs, while the cured variant, LR-163, showed no mortality and low CFU counts. LR-25 is thus classified as high virulent and LR-163, low virulent. Substantiation of the differences in virulence of this pair of strains was done by the release of oxygen metabolites from resident and activated mouse peritoneal macrophages. LR-25 triggered 45 and 135 n.moles of O_2^- and 20 and 22 n.moles of H_2O_2 from resident and activated macrophages; the corresponding figures for LR-163 were 82 and 238 for O_2^- and 38 and 58 for H_2O_2. Based on our earlier finding of an inverse correlation with virulence, these studies with oxygen metabolites confirmed the loss of virulence when the plasmids were removed from the MAC strain LR-25. In contrast to the association with virulence, no significant changes with respect to drug susceptibility were noted within the two strains.

WP.70 Clinical and Epidemiologic Characteristics of Non-AIDS HIV-Related Illness in NYC Hospitals

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The spectrum of HIV-related disease among hospitslized persons in New York City includes CDC defined A1 AIDS and other HIV-related illnessee (suspected AIDS). In order to describe the clinical and epidemiologic characteristics of this population of suspected AIDS cases, a point prevalence survey was conducted in March of 1986 at 25 hospitals that report 66% of AIDS morbidity.The average daily census at these hospitals for this month was 277 AIDS and 152 suspected AIDS cases. A total of 170 adult and 8 pediatric suspected AIDS cases were identified on the day of the survey. Of these, 35 were females and 143 males; 54% black, 19% white, 27% Hispanic. The major risk groups were; 104 (59%) IVDUs and 38 (21%) gay/bisexual men. The proportion of IVDUs among suspected AIDS cases was significantly greater(OR=3, p<0.01) than that among A1 cases reported from these hospitals during 1986 while the proportion of gay/bisexual men was significantly lower (OR=4, p<0.01). Seventy-eight (44%) of the 178 cases presented with pneumonic processes, primarily pneumonia, and 74 (42%) presented with oral thrush. Neurologic manifestations ranging from seizures to encephalitis were reported in 21 (12%) and CNS toxoplasmosis was suspected in 18 (10%). Prospective follow-up of this cohort of suspected AIDS cases has identified 29 confirmed adult cases to date. The distribution of cases by risk group is similiar to that in the original cohort. Oral candidiasis was the diagnosis most highly associated with the development of CDC defined AIDS (OR=2, p=0.004). These data indicate that persons infected with HIV, especially IVDUs, are a major burden on the health care system even before they develop confirmed AIDS.

WP.71 AIDS Surveillance in New York City

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AIDS Surveillance in New York City (NYC) serves as a model for surveillance programs nationwide. As of January 1987, 8887 cases of biopsy or culture proven opportunistic infections have been reported. The NYC AIDS Surveillance Unit receives approximately 270 cases monthly. Surveillance is conducted at 80 NYC hospitals and one prison infirmary. Facilities with high AIDS morbidity are visited weekly. Epidemiologic information is collected from personnel diagnosing and caring for patients. Cases under 13 years of age require contact with pediatricians. Charts are reviewed for details not obtained from physicians and nurses. Microbiology, pathology and death logs are reviewed for AIDS-associated illnesses. Hospitals with low morbidity are telephoned weekly. 83% of cases are reported from hospital personnel; 10% from medical records; and 7% from death certificates including autopsies.

Validation of the surveillance system is ongoing to ensure complete and timely reporting. Death certificates with AIDS-related morbidity are matched to cases or investigated as new cases. A weekly census of hospital beds utilized by AIDS patients measures the impact of the epidemic on NYC hospitals. Special attention is given to cases which define changing disease trends and patient characteristics. Patients denying homosexual activity and intravenous drug use or claiming occupational exposure are extensively investigated. Data is compiled and computerized in a system attentive to confidentiality and accuracy. Codes are assigned and names are removed.

NYC AIDS Surveillance is committed to an accurate description of the epidemiology of AIDS providing direction for programs in research, education and funding.

WP.72 Risk Factors for Human Immunodeficiency Virus (HIV) Infection Among Heterosexuals in New York City.

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Patients attending the sexually transmitted disease and gynecology outpatient clinics at Bellevue Hospital were invited to take part in a study of HIV risk factors and seroprevalence. Male patients with histories of intravenous (IV) drug abuse or homosexual activity were excluded from participation. Men or women with histories of blood transfusion since 1/1/77 also were excluded. Interviews and enzyme-linked immunosorbent assays for presence of HIV antibodies with Western blot confirmation have been completed for 76 males and 53 females. The mean number of sexual partners in the 12 months prior to interview among males was 5.9 (min. = 0, max. = 30) and among females was 3.3 (min. = 0, max. = 288). Three female participants acknowledged prostitution and 10 acknowledged IV drug abuse. Sexual intercourse with persons from AIDS risk groups was reported by 12 (16%) of the males and 21 (40%) of the females. Male subjects reported that only 12% of their sexual partners were protected by condoms during all sexual encounters. Women reported 100% condom use with only 2% of sexual partners. HIV seropositivity has been detected in 2 males and 2 females without AIDS risk factors other than heterosexual activity (equivalent to HIV infection rates of 2.6 and 4.3 per hundred, respectively). Three of 10 female IV drug users were HIV seropositive. These preliminary data suggest (a) that condoms are not being used by this patient population for disease prevention, and (b) that heterosexual spread of HIV is occurring. The study is continuing with a goal of recruiting substantially more subjects.

WP.73 Reactivity against $p24^{gag}$ in confirmatory assay for anti-HIV antibodies in low risk populations

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Among 5,000 serum samples of healthy volunteer donors used in a panel for testing ELISA kits for anti-HIV antibodies, 9 were found with reactivity against $p24^{gag}$ (and/or pr55) without reactivity against envelope proteins in Immunoblot analysis (IB) of HIV. Of 6/9 donors (2 females, 4 males) 37 sequential serum samples of donations going back to January 1984 were tested in IB and Radioimmuno-precipitation (RIPA). Upon extensive interviewing, no risk factors for AIDS were found. Of 2/6 donors also serum samples of 2 recipients of fresh frozen plasma could be tested. Sequential serum samples of the donors showed consistent reactivity against $p24^{gag}$ (with pr55 in one sample) from 1984 until July 1986 in 4/6 donors and marginal reactivity against $p24^{gag}$ in 2/6. RIPA was negative except for one sample ($p24^{gag}$). Virus cultures of fresh mononuclear cells remained negative in 6/6 donors during >40 days cocultivation. Two patients receiving fresh frozen plasma of 2 donations positive for $p24^{gag}$, remained negative 6 months after transfusion, as tested by ELISA (2 kits) and IB. In Immunoblot Assays with HTLV-4 and LAV_2/HIV_2 encoded proteins, none of the donor samples showed reactivity consistent with HTLV-4 or LAV_2/HIV_2 infection, i.e. envelope glycoproteins (P. Kanki, M. Essex, dept. of Cancer Biology Harvard University Boston, U.S.A., Diagnostic Pasteur, Marnes la Coquette, France). Reactivity against $p24^{gag}$ of HIV in IB can persist for at least 2 years without signs of HIV-infection. In low risk populations this reactivity represents false positivity.

WP.74 Increasing Incidence of Tuberculosis in a Prison Inmate Population: Association with HIV Infection

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Concurrent with the AIDS epidemic, tuberculosis incidence rates in prison inmates in New York State have risen 360% from 15.4 per 100,000 in 1976-78 to 70.9 per 100,000 in 1984-86 (provisional incidence of 105.5 in 1986). At the same time, AIDS incidence in inmates increased from 8.4 per 100,000 in 1981 to 289.6 per 100,000 in 1986. To investigate the association between the large increases in these two diseases, we reviewed data from New York State's AIDS and TB registries.

Over the past six years, 347 cumulative AIDS and 112 cumulative TB cases have been reported in inmates. No geographic clustering of TB cases was noted. Six percent of AIDS cases have had TB, and 20 percent of TB cases have had AIDS. By year of AIDS diagnosis, the number of AIDS cases with TB has increased from 0 in 1981-82, to 7 in 1983-84, and to 15 in 1985-86.

Of the 54 TB cases reported in 1985-86, 15 (28%) had AIDS, 15 (28%) additional cases were HIV seropositive, and the remainder had unknown HIV antibody status. There were no reported seronegatives. Twenty-one (39%) of the 54 had extrapulmonary TB, a finding often associated with HIV infection.

These findings document an increasing rate of TB in prison inmates and strongly suggest its association with HIV infection. Standard TB control efforts should be intensified in order to reverse this increase in TB rate.

WP.75 HIV ELISA Results in Heterosexual Partners of Persons at High Risk for HIV Infection.

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We have offered free confidential HIV counseling and testing (ELISA and Western Blot) in conjunction with the NYC Department of Health for a large urban population since 9/85.

Of the 430 patients that we have tested, 128 were heterosexual partners of bisexual men or intravenous drug abusers. None of these 128 individuals used "safe sex" methods. Ninety-six were women and 32 were men. Five of 96 women and 0/32 men had symptomatic HIV infection (AIDS, ARC or GLA). Twenty-eight of 128 (21.9%) patients tested positive for HIV antibody, with confirmatory Western Blots. Sixty of 96 (62.5%) women and 11/32 (34.3%) men reported sexual contacts with known HIV infected partners [AIDS, ARC] since 1983. Twenty-two of 60 (36.6%) of the women and 3/11 (27.2%) men exposed to partners known to be HIV infected were HIV antibody positive. In comparison only 1/36 (2.8%) of the women and 2/21 (9.5%) of the men who reported heteroaexual contact with high risk partners without evidence of symptomatic HIV infection were HIV antibody positive. While 36% (8/50) of the women whose reported risk was with high risk husbands were HIV positive, only 5/46 (10.9%) of the women having had sex with high risk boyfriends tested positively.

Heterosexual contact with high risk group individuals who are symptomatic for HIV infection carries a significantly higher risk of infection than contact with non symptomatic individuals. Women who have had long term relationships with members of high risk groups are more likely to be infected with HIV than those with short term relationships.

WP.76 Clinical Course of HIV-seropositive Homosexual Men
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Estimates for progression to overt AIDS among HIV-seropositive(HIV+) homosexual men(HM) have varied from 10% to >30%, with an apparent increasing risk over time. We report follow-up on a cohort of 178 HIV+ HM enrolled in 1982-4. One hundred and seventy-eight(78%) were selected for the presence of persistent generalized lymphadenopathy(PGL); the rest were asymptomatic and had no PGL. Follow-up was 3-56 mo(median 42 mo). Twenty-five(14%) developed AIDS, an annualized rate of 4%; the annualized rates were 5% for HIV+HM with PGL(N=22) and 2% for HIV+HM without PGL(N=3). Using the date of documentation of HIV seropositivity, the risk of AIDS was higher at 4 yr than 1-3 yr, (P=0.03). Compared with the 153 HIV+HM who did not develop AIDS, the 25 who developed AIDS had lower initial T4 cell counts(mean 285 vs 557/mm^3, P<0.001), lower T4:T8(0.38 vs 0.77,P<0.001), and were more often anergic at enrollment(11/16 vs 34/127, P=0.001). There were no differences in age, constitutional symptoms, presence of PGL, initial hematocrit, T8 or total lymphocyte counts. In addition, 12 subjects have developed oral candidiasis or ARC. The risk of overt AIDS among HIV+HM appears to increase over time; the relatively low rates in this cohort compared with reports from San Francisco or New York may reflect a more recent introduction of HIV into Seattle.

WP.77 A THREE YEAR SURVEY OF ANTIBODY RESPONSE TO HIV ANTIGENS IN THE CENTRAL AFRICAN REPUBLIC.
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A three-year survey for HIV 1 antibodies in several population groups of the Central African Republic was conducted between October 1984 and January 1987. This survey included 1,663 persons from randomly selected households in Bangui, or seeking medical care in the Pasteur Institut; two groups of 377 and 930 people, aged 15-34 and one group of 320 children aged 0-14 all randomly selected from the urban population; 830 people selected from the rural population; 234 hospitality girls from low and middle socio-economic status; 100 tuberculosis in-patients; 175 malnourished children along with 101 mothers; and 396 pygmies from two separate pygmy tribes. All sera were screened using ELISA technique, then confirmed by Western Blot, and considered positive only if either GP110 or GP41 or both were present.

Results were as follows: the prevalence of anti HIV 1 antibodies in the general population ranged between 2.1 and 4.04 in separate surveys conducted 18 months apart: an insignificant range (Chi square: 2.4). Among hospitality girls the range was between 20.6 and 12, again separated an 18-month interval. Anti HIV 2 antibodies were found to be present both in the urban and pygmy populations.

The striking feature of these surveys is a lack of increased incidence in HIV 1 antibodies particularly among the prostitutes examined through a 18 month period.

WP.78 A.I.D.S. SURVEY IN CAMEROON
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Since May 1985, 25 patients affected by AIDS have been detected by Pasteur Center of Cameroon (8 men, 17 women). 3000 serological tests were performed during several epidemiological surveys among the cameroonian populations.

Each positive case was confirmed (RIPA Cystein or Western Blotting).

Different types of surveys were carried on:

- Household cluster sample surveys on randomly selected populations in urban areas:
  - . in adults the prevalence of antibodies carriers is 0.6% (11/1761).
  - . in children under 15 the seroprevalence is 0% (0/319).
- Sample surveys among out-patients in Yaounde and Nkongsamba:
  - . 488 sera tested, none is positive
- Surveys among high risk groups:
  - . 358 hospitality girls have been tested, with 10 positive cases (2.8%), 3 of them being cameroonian.
- No positive sample among 40 sickle cell anemia polytransfused patients followed in Yaounde.

Throughout the Cameroon Republic, AIDS prevalence among the healthy population is therefore about 0,5% confirmed cases.

The number of false positive immunoenzymatic tests should be noted (72%).

WP.79 Sero-prevalence of anti-HIV antibodies in Brazzaville (Congo).
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Congo is located in Central Africa, West of Zaïre. The first cases of AIDS were reported in 1983. Blood-bank screening for anti HIV antibodies is completed since July 1986. A commercial ELISA kit (ELAVIA, Diagnostic Pasteur) is used and 4 387 blood donnors were tested between July 1986 and December 1986 among which 269 were repeatedly reactive (10,13 %).

During November and December 1986, sera of in-patients were systematically tested and 245 out of 654 were repeatedly reactive (37,4 %). One hundred and thirty five had AIDS, according to WHO clinical score for Africa. Western blot could not be done because of lack of local facilities.

WP.80 Prospective study of the vertical transmission of HIV.
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In a ongoing study to evaluate vertical transmission of HIV, peripheral and cord blood is obtained at delivery from pregnant women with HIV infection and tested for HIV antibodies (Ab) and antigens (Ag). Infants are followed up clinically and tested at three months intervals for HIV Ab and Ag as well as for T cells subsets. Since October 1985, 8 seropositive women have been studied : 3 were IV drug abusers and 4 were of african origin ; HIV Ag were detected in the peripheral blood of 4/8 at delivery. Of the 8 infants (mean birth weight 2618 gr, range 1620-3500 gr), 2 were born prematurely. HIV Ab were present in cord blood from the 8 infants but Ag was detected in only 1/8. At this writing, follow up data is available for 7 infants for a mean period of 9.5 months (range 1-16 months). None of them has clinical or immunological signs of HIV infection. Two infants now 15 and 16 months of age, born to seropositive Ag negative drug abusers, have had repeated negative tests for HIV Ag and have no more Ab detectable suggesting that HIV has not been transmitted. The infant whose cord blood was positive for HIV Ag is now 12 months old and clinically healthy. At his 9 months follow up visit, T cells subsets were normal, HIV Ag was present, but Ab were not detectable by Elisa or IF ; WB was only positive for P 24 and P 53. Ag was detected at the 6 months visit of an infant whose cord blood was negative. The 3 youngest infants have not yet been retested. These results indicate that, in addition to careful clinical and serological follow up, the study of the vertical transmission of HIV requires testing for the presence of HIV Ag.

WP.81 Prospective Evaluation of HIV-associated Morbidity
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The natural history of HIV-infection was studied prospectively in 142 patients (pts), who were examined at least twice during a minimum period of 6 months. Median follow-up period was 10 (range 6-37) months. The CDC classification system for HIV-infections was used. Initial diagnoses were: Asymptomatic infection ± laboratory abnormalities (II A+B) in 46 pts (32%); persistent generalized lymphadenopathy (LAS, III A+B) in 46 pts (32%); constitutional symptoms and minor opportunistic infections (IV $A+C_2$) in 32 pts (23%); and AIDS (CDC surveillance definition, IV C_1+D) in 18 pts (13%).

From group II 14 and 5 pts progressed to groups III and IV, respectively. In contrast, only 7 pts deteriorated from III to IV ($p < 0.01$). Within group IV $A+C_2$ 6/32 pts (19%) developed serious opportunistic infections or tumors (--> IV C_1+D). Overall, AIDS developed in 9/124 pts (7%) after 4-24 months, including those 6 pts from group IV $A+C_2$. A comparative analysis of progression rates (Kaplan-Meier method) showed - despite similar observation periods - that pts in group II had a significantly higher risk ($p < 0.01$) for deterioration than pts in group III. 13/27 pts with AIDS died, all of them had prior opportunistic infections (IV C_1).

Thus, 32/142 (22%) pts had evidence of progressive disease during this limited follow-up period. We conclude that HIV-associated morbidity - even for asymptomatic pts - is high.

WP.82 Update: Racial Differences between Patients with Hemophilia-Associated AIDS in the United States, 1981-1986.

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As of December 15, 1986, a total of 281 cases of hemophilia-associated AIDS had been reported to CDC. These cases represent a cumulative incidence rate of 1.6 AIDS cases per 100 persons with hemophilia. The number of AIDS cases diagnosed annually has nearly doubled, except in 1986, during which cases increased only 10%; however, reporting is not yet complete for that period. Demographic characteristics of the patients diagnosed each year have not changed significantly. The majority of patients had severe hemophilia A (66%) and had received commercially produced clotting factors (98%). Of the 281 patients, the proportion of blacks was significantly lower than that of blacks in the general U.S. population (8% [22/281] vs. 12%, p=0.005). The median age for black patients was significantly lower than that for white patients (26 years vs. 34 years, p=0.02). Significantly more black than white patients had mild or moderately severe hemophilia (9/19 [47%] vs. 51/216 [24%], p=0.02). Black patients were more likely than whites to have received plasma or packed red blood cells in addition to commercially produced concentrated clotting factors (7/17 [41%] vs. 49/203 [24%]); however, the difference was not significant. These data suggest that AIDS is diagnosed less frequently among black hemophiliacs than white and are consistent with a higher early mortality rate among black hemophiliacs due to their coagulation disorder or the presence of racial cofactors for the development of AIDS. However, population-based studies are needed to better define these racial differences.

WP.83 A Three Year Prospective Study of Initially Asymptomatic HIV Positive Gay Men in Stockholm, Sweden.

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In a health screening project in Stockholm, Sweden, consecutive asymptomatic gay men have been enrolled and prospectively followed since Nov 1982. Frozen coded sera from 998 men, drawn during the period Nov 1982 to Dec 1983, have been examined for serum antibodies to Human Immunodeficiency Virus (HIV) by ELISA. Positive reactions were confirmed by Western blotting. The seropositive men have been followed and their clinical status three years later is presented. Repeated determination of T cell subsets were done in most men.

Results: HIV antibodies were demonstrated in 123 (12.3%) of the 998 men. Of the seropositive men it was possible to evaluate 116 men after a mean time of 40.6 months. Of these 116 men, 19 (16.4%) had developed AIDS. Eleven of the men with AIDS had died. Of the men without AIDS it was possible to clinically evaluate 80. Of those, 8 (10.0%) had AIDS Related Complex (ARC), 38 (47.5%) had Persistent Generalized Lymphadenopathy (PGL) and 33 (41.3%) had a minor lymphadenopathy (ML) or were completely asymptomatic. One man (1.2%) had died of and one man with ML had been treated for Malignant melanoma. Of the men diagnosed as having AIDS, 8 had Pneumocystis carinii pneumonia, 5 Kaposi's sarcoma (KS), 2 CMV infection, 1 Candida esoephagitis, 1 Toxoplasmosis, 1 Cryptococcus meningitis and 1 both KS and Lymphoma at the time of diagnosis.

Conclusion: This study shows that the morbidity and mortality of HIV infection is high even in recently infected individuals living in a country with a high standard of living and good health services like Sweden. T cell subsets as prognostic markers will be discussed.

WP.84 Antibodies to HIV in Cervical and Oral Secretions of Female Prostitutes in Zaire

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The antibody response to HIV in cervical and oral secretions was studied in a cohort of high risk African individuals. The population assayed consisted of HIV seropositive and seronegative active female prostitutes from Zaire. Oral secretions were collected by rinsing the subjects' mouths with PBS followed by expectoration. Cervical secretions were collected by adding a cervical scraping to an aliquot of PBS. Secretions were assayed for antibodies using a modified,IgA-enhancing radioimmunoprecipitation of ^{35}S-cysteine-labeled Molt HIV-infected cell lysates.

Seventeen of 22 cervical samples and 19 of 22 oral samples from the seropositive individuals contained antibodies to viral antigens. Antibodies to gp160, gp120, and p24 were consistently found. One seropositive individual had no detectable antibodies in either secretion. Secretory antibodies were not detected in the oral secretions of 21 seronegative individuals. One of 21 cervical from seronegative prostitutes showed a weak precipitation of gp160 and 120. We have demonstrated that 21 of 22 serpositive women possess viral-specific antibodies in their oral and/or genital secretions. The presence of antibodies at mucosal surfaces may be associated with the lower incidence of female to male transmission of AIDS.

WP.85 Serial Western Blot Analysis in the Early Diagnosis of HIV Infection

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Ten individuals (2 males and 8 females) presented for testing following repeated heterosexual exposure to an HIVpositive partner. Last intercourse had occured 6 months to several days before testing. Only 1 patient was initially reactive by ELISA (Abbott). Western blot analysis revealed a weak p24 band in one case (#1) and a weak p55 band in two other cases (#2 and 3). In each case the absorbance value of the ELISA was clearly negative. All but one patient agreed to return for a regular follow-up which included HIV antibody testing, viral culture and an extensive immune profile. Patient 1 did not return for evaluation before 6 months. At that time ELISA and Western blot were strongly positive. Patients 2 and 3 were evaluated 3 months later. In both cases bands reactive to all gag protein antigens were identified by Western blot, while the ELISA test was still negative. Viral culture was negative in both cases. All the other patients have remained negative by both ELISA and Western blot when tested 1 to 4 times over a period of 3 to 15 months. In all 9 patients the immune parameters were within normal limits. These results suggest that serial Western blot analysis which does not overlook weak p55 and/or p24 bands is the most sensitive way to diagnose early HIV infection.

WP.86 Immunological Progression of HIV Infection in Sydney Gay Men--A Generalised Linear Model

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Over a period of three years, the Sydney AIDS Prospective Study has collected epidemiologic, clinical, serological and immunological data, in six-monthly visits, from over 1000 homosexual men, of whom 40% are HIV ABV positive. In over 85% of the HIV ABV positive subjects, this longitudinal study finds the linear sequence immunological progression of the disease to be low T4/T8 ratio, low T4%, to low T4 count, and finally low lymphocyte count, confirming the stages found by Zolla-Panser in a cross-sectional study. A very significant correlation was found between this progression and the rate of change of T4 cell count with respect to time, suggesting that each step in the progression is determined predominantly by T4 changes.

Each of the stages of immunological progression where analysed in relation to clinical features which varied from asymptomatic to LAS, ARC, and AIDS. Using logistic regression and linear modelling tools, no correlation was found between clinical and laboratory findings, nor between lifestyle factors and immunological progression. The highly variable relationship between clinical findings and immunological changes indicate that a much more complex branching model of the disease is needed to predict outcome.

WP.87 HIV Infection in Dialysis Centres.

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A prospective multicentre study was undertaken between February 1985 and August 1986 in 4 haemodialysis centres in the Paris area (France) in order to assess the prevalence of HIV infection and the risk of transmission of the virus within the centres. A four-month follow-up was carried out in 221 patients undergoing haemodialysis (HD) and in 40 staff members caring for the patients in 2 centres. 62 patients undergoing peritoneal dialysis (PD) and 126 haemodialysis patients who transited through a centre (HDT) were screened once. A questionnaire exploring risk factors was completed for each patient and staff member. Sera were tested for HIV antibodies by ELISA (ELAVIA) and confirmed by Western Blot. Of the 357 HD+HDT patients, 4 were found to be positive. Of the 221 HD patients, 1 multi-transfused haemophiliac and 1 multi-transfused Nigerien without other risk factors were positive in the first screening. Another patient seroconverted after transfusion during the study; no other risk factors existed and the donor has not yet been found. One of the 126 HDT patients had received infected plasma. No staff members or PD patients were positive. No transmission within centres, from patient-to-patient or patient-to-staff was evidenced. Although HIV seems to be less infectious than HBV, precautions to prevent transmission of HIV in dialysis centres should be maintained.

WP.88 The Impact of Presumptively Diagnosed Opportunistic Infections and Cancers on National Reporting of AIDS

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A review of death certificates in four U.S. cities suggested that at least 10% of AIDS cases do not meet the national surveillance case definition because of the lack of biopsy or other specific confirmation of the indicative disease and are therefore unreportable. To assess the frequency of the resulting underreporting, health departments in five areas of the United States reviewed medical records for all or for a random sample of patients treated during a fixed time period who 1) had previously been considered as suspected AIDS patients and/or 2) had discharge diagnoses consistent with the various AIDS indicative diseases. Extrapolations from preliminary results in four areas suggest that 96 AIDS cases were presumptively diagnosed during the same period that 723 cases were definitively diagnosed, for an overall 11% rate of presumptive diagnoses, ranging by area from 4% to 15%. Information from the fifth area suggests the rate there may exceed 50%. Coincidentally, the studies identified 58 (7%) previously unreported AIDS cases that meet the national surveillance case definition, consistent with results from validation studies elsewhere. When data analysis is completed in March, we will estimate the impact on national AIDS surveillance of not reporting presumptively diagnosed AIDS cases. The study will also 1) identify reasons presumptive rather than definitive diagnostic methods are used, 2) determine which opportunistic infections and cancers are presumptively diagnosed most often, 3) indicate trends over time in the frequency of presumptive diagnosis, and 4) estimate the usefulness of retrospective chart review in identifying unreported AIDS cases.

WP.89 CD4 + cells' count as predictive marker of disease progression in HIV-positive parenteral drug addicts.

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CD4 + cells' count in peripheral blood is considered a valuable predictive marker of clinical evolution in HIV infections. A clinical survey of 375 parenteral drug addicts (PDAs) examined between 1984 and 1986 was performed. All studied subjects (279 males, 96 females, age ranging between 18 and 33) sharing behavioural, social and toxicomanic habits, live in Milan, where the first HIV seroconversion in PDAs was documented in 1979. A clinical classification was made following CDC's and Walter Reed Foundation's criteria. T cell subsets were determined by an Ortho spectrum III cytofluorograph. Mean counts of CD4 + cells in the overall population showed a significant decrease during the three years of the study (from 986.5 $\pm$ 642.1 in 1984 to 491.9 $\pm$ 244.3 in 1986, $p < 0.001$). In order to evaluate decreasing chances (below 400/mm^3) of CD4 + cells in 108 already symptomatic patients, we considered as conventional starting point for a subsequent follow-up the onset of a histologically confirmed lymphadenopathy syndrome (LAS). Once diagnosis of LAS was made, CD4 + cells' chances of decreasing below 400/mm^3 were 50% after 32 months. Our data confirm on the one hand the trend to a rapid decrease of peripheral CD4 + cells in the overall population of HIV infected PDAs, on the other hand, the relatively long average time required by CD4 + cells to reach levels below 400/mm^3 in symptomatic subjects, pointing to a possible slow progression of the disease.

WP.90 A Computer Model of the AIDS Epidemic

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This model tracks the spread of AIDS through the sexually active population, quantifies the effect of such disease carriers as intravenous drug users, bisexuals, and hemophiliacs, predicts infection and mortality, and evaluates the sensitivity of the epidemic to policy and behavioral changes. These include improved educational programs, changes in sexual habits, provision of sterile needles to intravenous drug users, application of disease-inhibiting drugs, implementation of testing programs, and reduction of the likelihood of disease transmission through prophylaxis.

The model divides the sample population into three categories: homosexuals, bisexuals, and heterosexuals. Each category includes intravenous drug users and hemophiliacs. The transmission of AIDS through sexual interaction, needle sharing, and blood transfusions is characterized by a set of non-linear equations which are solved using the STELLA simulation language on an Apple Macintosh microcomputer. When quantified by United States aggregate data from the National Centers for Disease Control, the model predicts a peak in the AIDS-infected population in 1991 accompanied by the devastation of the bisexual and intravenous drug using populations, and demonstrates the relative insensitivity of the epidemic to increased sexual frequency and to increased number of partners.

We will show how to apply the model to a particular region by describing a ten-year simulation of AIDS in New York City.

WP.91 Women with the Acquired Immunodeficiency Syndrome in Miami

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Miami reports the fifth highest number of cases of AIDS in the United States, including one of the highest percentage of women with AIDS. During the past 3 years, 111 women were diagnosed with AIDS at our medical center. Ten were caucasian and 101 were black, ranging in age from 20 to 57 years. Risk factors for AIDS included intravenous drug abuse (43), heterosexual contact with a person at risk for AIDS (8), blood transfusions (7), and 50 women of Haitian ancestry. The number of cases and associated risks factors per year are listed below:

Years	Number	Intravenous Drug use	Heterosexual contacts	Blood Transfusion	Unknown	Haitian ancestry
1983	17	4	1	1	0	11
1984	17	9	1	1	0	6
1985	31	12	3	2	1	13
1986	46	18	3	3	2	20

Ninety-eight presented with opportunistic infections including 31 with multiple infections, 14 with opportunistic infections and Kaposi's sarcoma, and one each with Kaposi's sarcoma or lymphoma. The types of infections included: P. carinii pneumonia (73), toxoplasma encephalitis (21), M. avium-complex infection (7), cytomegalovirus infection (10), Cryptococcosis (10), and Cryptosporidiosis (9). Associated infection with oral thrush (63), genital herpes (32), and herpes zoster (4) were also found. Six women presented with AIDS during pregnancy, and 18 reported a history of miscarriage. The average length of survival after diagnosis was 6.6 months, ranging from 1 to 23 months. AIDS among women appears to be increasing, is disproportionately associated with multiple infections and has a poor outcome.

WP.92 The Melbourne Cohort After 3 Years: Halt of Sero-conversion to HIV and Predictors of Immune-Deficiency.

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In 1983 a cohort of 100 asymptomatic homosexual men was recruited for a prospective study. HIV seroconversion and immune function assessments included T Lymphocyte subsets, including helper-inducer (CD4 + 4B4) and suppressor inducer (CD4 + 2H4+) cells, serum immunoglobulins, and capacity for recall of delayed hypersensitivity.

The prevalence of antibody to HIV rose from 22% in 1983 to 31% (24/78) in 1985. There has been no further seroconversion in 1986, suggesting that the spread of virus into and within this group has been halted.

We have analysed the immunologic parameters from visits 1-8 to determine whether there are continuing group trends, single measurements are predictive, or whether for a single individual serial measurements have better predictive value. For T helper (Leu 3) subset numbers, correlation analysis between visits followed by simple linear regression was not significant ($p=0.15$). However, t tests for repeated measurements on same individuals was significant in the seropositive group ($t=2.18$, $p=0.03$). Similarly, for serum immunoglobulin concentrations, only the t test for repeated measurements in the seropositive group was significant ($t=3.59$, $p=0.002$). These results indicate that although there are clear group trends, for a single indivual, serial and not point-measurements are necesssary to predict immunodeficiency.

WP.93 Novel Phenomena in Epidemics Associated with Long Incubation Periods: Application to AIDS

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The onset of any epidemic associated with a disease having long incubation periods displays a behavior which is well-known from acoustics and electronics: a transient appears, meaning that the pattern of the observed epidemic does not mirror exactly the spread of the infectious agent during an initial phase of the order of the breadth of the incubation period distribution. For instance, a fictitious disease having an incubation period between 1 and 5 years with a mean incubation period of 3 years whose agent (a virus, say) spreads with a constant doubling time of 12 months leads to an epidemic starting with a doubling time of only 6 months. The doubling time of the observed numbers of cases increases during a 5 year period until it becomes equal to the doubling time in the number of virus carriers (12 months).

Such an onset transient is very important for AIDS. Here, the extremely long mean value and the large variance of the incubation period distribution imply that during an initial stage which may last up to 7 years most of the observed increase in the doubling time of AIDS cases is a spurious effect. This is shown with numerous examples for different compartments and countries.

Genuine drops in the rate of spread of HIV induce again negative transients which must be taken into account in order to achieve a real understanding of the epidemic pattern.

WP.94 Evidence for Heterosexual Transmission of HIV in the United Kingdom
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Heterosexual transmission of HIV is presumed to have occurred in 18/610 (3%) AIDS cases and in 48/3870 (1.2%) HIV antibody positive individuals reported to CDSC between 1982 and 1986.

The 18 AIDS cases were associated, predominately, with people whose heterosexual contacts or residents were abroad (14/18). The other four cases were 'UK acquired': One case from a haemophiliac, the second case a prostitute with American contacts, the third was an African living in England since 1963, and the fourth was a male with multiple partners, including prostitutes, but who had shared razors with drug users. The 48 HIV antibody positive individuals most probably contracted their infection as follows: 15 from haemophiliacs (31%), 8 from contacts abroad (17%), 6 from prostitutes within Europe (13%), 5 from contact with IV drug abusers (10%) and four from AIDS cases or HIV antibody positive husbands: One had a boyfriend with American contacts; one was a wife of a bisexual man, two had a history of prosmiscuity, one with Dutch contacts; and 5 individuals from whom the contacts are still being sought.

Four groups make up 79% (52/66) of the reported heterosexually acquired infections; the British visiting or living in Africa (19/66), and the partners of haemophiliacs (16/66), prostitutes and their contacts (8/66) and the sexual partners of IV drug users (5/66). The AIDS cases and HIV infections occurred 1 in 1982, 4 in 1983, 3 in 1984, 16 in 1985 and 42 in 1986. The actual number of heterosexual infections is unknown but this data is unequivocable. The 'heterosexual' outbreak of AIDS has started in the UK. Surveillance and practical intervention will be discussed in the context of these findings.

WP.95 HIV INFECTION AMONG FEMALE AND MALE PROSTITUTES. U.Tirelli, E.Vaccher, S.Diodato, R. Bosio, P.De Paoli, O.Crotti et al. AIDS and Related Syndromes Study Group. Centro di Riferimento Oncologico, Aviano, Italy.

Between September 1985 and January 1987, we carried out a prospective study in 36 female prostitutes, 22 of whom were intravenous drug abusers (IVDA), and in 15 male prostitutes, 3 of whom were IVDA, 9 transvestites and 3 homosexual men, in Pordenone and Treviso, two towns of North-East Italy. The prostitutes were clinically examined, given laboratory tests including HIV antibody tests (Elisa with Western Blot confirmation) and T4/T8 ratios and completed a questionnaire on their sexual behaviour. Results:

	FEMALE PROSTITUTES		MALE PROSTITUTES	
	IVDA (n=22)	NON-IVDA (n=14)	IVDA (n=3)	NON-IVDA (n=12)
Median age (yr)	24	37	26	25
Median duration of prostitution (yr)	2	10	1	8
Median partners / mo	70	90	NA	150
Rectal intercourse	4%	7%	100%	100%
Frequency of:				
HIV antibody	59%	0%	33%	8%
AIDS	0	0%	0%	0%

Our data shows that female prostitutes who are not IVDA and male prostitutes who are not homosexual are not at increased risk for AIDS while female and male prostitutes who are IVDA should be considered at risk for HIV infection.

WP.96 Immunological, Serological and Clinical Abnormalities in Children Born to Promiscuous and Drug-Addicted Mothers at Risk for AIDS.
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Two different enzyme-linked immunoassays and indirect immunofluorescence or Western blot tests were used to evaluate HIV seropositivity in 201 I.V. drug abusers. In this population, 89% (71% males and 18% females) were considered to have HIV antibodies. We studied 45 infants and children (ranging from 1 month to 6 years of age) born to drug-addicted and sexually promiscuous mothers. Thirty-six percent were found to be HIV-positive. Furthermore, 9 of 15 children born to drug-addict mothers (60%) and 3 of 20 born to sexually promiscuous (10%), were seropositive. The other 4 affected children were born to heterosexual mothers with partners in the at-risk groups. Twenty-nine (64%) were HIV-negative children without clinical signs, but with increased (43%) and decreased (29%) T4/T8 ratio, reduced PWM response (50%), but normal serum levels of Igs. The other 16 were HIV-positive, and of these 4 (24%) had asymptomatic infection and 12 (75%) were included in group IV as clasified by CDC (2 had AIDS, 7 had ARC and the other 3 were group IV-E). In the HIV-(+) group all children showed a significant increase of IgG as compared with HIV-(-) group ($p<0.01$), and there was a significant difference in IgA levels between HIV-(+) group IV and HIV-(+) asymptomatic children ($p<0.05$). All HIV-(+) children in group IV showed a progressive drop in T helper cell numbers (89%) and T4/T8 ratio (100%) and decrease in blastogenic response to PWM (100%). Children of the HIV-(+) group IV also showed infection by other viruses (20% were HbsAg-(+) and 33% had antibody to hepatitis B core antigen). Of special note is the fact that in children of the HIV-(+) group IV, 69% had been immunized with the usual vaccines as compared with only 25% in the asymptomatic HIV-(+) group. Further investigations are in progress to elucidate which co-factors might be involved in the evolution of AIDS in children at-risk.

WP.97 Utilization of the Highly Permissive C3 Cell Line in Rapid Serum Neutralization Assays.
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The HTLV-II transformed cell line C3 is highly permissive to HIV infection in vitro. Even in the presence of low MOI (0.01-0.1), this cell line exhibits rapid expression of viral antigens in 4-6 days with extensive cell lysis as early as 7-9 days post virus adsorption. Utilizing the C3 cell line, a rapid neutralizing antibody screen is now described. Demonstrated are results derived from patient sera obtained during the course of antiviral drug therapy. Using either an increase in time to cytolysis, reduction in reverse transcriptase assay values, or reduction in percent indirect immunofluorescence as the criteria for neutralization of virus, it is possible to clearly demonstrate significant differences in the anti-HIV qualities of different patient sera. Some patients show significant neutralizing ability with either percent fluorescent cells or reverse transcriptase levels less than thirty percent of HIV infected control. Other patients show virtually no ability to neutralize HIV with RT assay values or percent fluorescence eighty percent of control values. Therefore, utilizing standard neutralizing antibody titer techniques but incorporating the C3 cell line, it is possible to completely evaluate patient serum in seven days. The rapidity with which this cell line expresses viral antigens makes the C3 the cell line of choice in serum testing especially when large numbers of sera must be evaluated.

WP.98 Cleavage of C3 Complement in the Serum of AIDS or AIDS Related Complex (ARC) Patients
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C3 deficiency leads to chronical diseases. It was extremely interesting to study C3 in patients with AIDS.27 sera of AIDS and ARC patients were examined by Western blot analysis using 125 I labeled anti-C3 monoclonal antibodies (LBP G10) specific to native C3 molecule and its C3a fragment (Mr=9,2kD). In 26 sera C3 protein bands were detected at a level of few percents and in one case its amount was about ten percents of that in normal serum. In 20 sera two intense bands, corresponding to Mr=9.2kD and Mr=8.3 kD were found. The latter fragment was not previously described in the process of C3 cleavage. In two sera only this fragment was detected and 5 sera did not contain C3a specific fragments at all. In some sera the other C3a containing fragment with Mr=140 kD was present. C3 component may be cleft by the virus and/or cell protcases produced during cell destruction. Enhanced cleavage of C3 complement component may be a new important factor in the development pathogenicity of HIV induced immunodeficiency.

WP.99 Failure to Demonstrate HIV-Specific CTL in Asymptomatic Antibody-Positive Homosexual Men.
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We have attempted to generate human immunodeficiency virus (HIV)-specific cytotoxic T-lymphocytes (CTL) from 18 antibody-positive asymptomatic homosexual men. This population has been shown to have elevated numbers of cytotoxic precursor cells (Leu 2^+, Leu 15^-). The mean $CD8^+$ cell number of the group studied was 839 ± 346 per mm^3 (normal range 192-726), with 50% being above the normal range. Sixteen had an inverted CD4/CD8 ratio (x=0.77) and the mean $CD4^+$ cell number was 633 ± 259 per mm^3 (normal range (468-1433).

PBL were cultured with live virus for 7-14 days, then assayed for killer activity on infected autologous monocytes, infected autologous $CD4^+$ PHA-stimulated blasts, or $CD4^+$ PHA-stimulated blasts with virus bound to the cell surface. In some experiments we added either IL-2 or irradiated allogeneic PBL to the culture in an attempt to supply any factors necessary for CTL production. We also tried to restimulate primary cultures with irradiated HIV-infected autologous PHA-stimulated blasts. We detected no HIV-specific CTL under any of these conditions. Cultures with infectious HIV did not abrogate the generation of EBV-specific cytotoxic cells from normal individuals. Since CTL specific for other human viruses, such as influenza, EBV and CMV, are generated under similar conditions to these, we conclude that under conditions that normally allow CTL generation in humans, HIV-specific CTL are not detectable.

WP.100 Mice Depleted In Vivo of "T4" Lymphocytes Do Not Die of Infection With Ectromelia Vaccinia or Cytomegalovirus

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Many AIDS patients do not generate in vitro T cell responses to virus (self restricted antigen, S+X), but exhibit elevated T cell responses to HLA allo-antigens (ALLO) (J. Immunol. 137:2514, 1986). Terminal AIDS patients, however, appear to have also lost their in vitro ALLO responses. This difference raises the possibility that the $CD4^-$ T cell pathway responsibile for the ALLO reactivity provides some protection in AIDS patients. Murine in vitro T cell responses to (S+X) require $L3T4^+$ (CD4) helpers, whereas ALLO responses can be generated by $Lyt2^+$ (CD8) helper cells (J. Exp. Med. 162:427, 1985).

Because of this similarity in the T helper pathways of the two species, we have tested the possibility that mice depleted in vivo of either $L3T4^+$ or of both $L3T4^+$ and $Lyt2^+$ cells will be susceptibile or resistant to the murine pathogenic viruses ectromelia, vaccinia, and cytomegalovirus (CMV). Mice in which both T cell pathways were intact generated T cell and antibody responses to these viruses and were resistant to the infections. Mice depleted of both L3T4 and Lyt2 cells did not generate T cell or antibody responses and died soon after exposure to ectromelia or CMV. However, mice selectively depleted in vivo of L3T4 cells and subsequently infected with ectromelia, vaccinia or CMV generated T cell responses, did not make antibodies, but did not die from virus infection. Further, studies of the CMV infected mice indicated that CMV could be detected in the salivary glands and spleens of mice depleted of $L3T4^+$ cells or of both $L3T4^+$ and $Lyt2^+$ cells, but virus was much more extensive in mice depleted of both subsets. These in vivo studies of selective "T4" depletion in mice raises the possibility that the elevated T4 independent pathway provides some immune protection in the AIDS patient.

WP.101 Further Investigation of a Suppressive Factor Associated with HIV.

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We and others have earlier shown that a purified Triton-X treated extract of $HTLV\text{-}III_B$ suppress the lymphocyte transformation response of normal lymphocytes to mitogens and antigens, whereas an extract of uninfected H9 cells do not. We have now shown that the suppressive factor is also present in non-Triton-X treated virus preparation and in preparations from the MB6 cell line known not to be mycoplasma-infected, which exclude these trivial explanations for the suppression. Moreover, the extract did not contain demonstrable amounts of tumor necrosis factor or lymphotoxin indicating that it is not of cellular origin. It suppresses all cells studied of hematopoietic origin, including the formation of colony forming units from human bone marrow, but not fibroblasts. It has a MV of about 70.000 on Sephadex separation. Preincubation of lymphocytes with the extract before adding mitogen gives pronounced suppression, while addition of extract three days after mitogen has little effect indicating that the factor acts early. It compleately inhibits IL-2 receptor expression. It's action cannot be blocked by addition of IL-1, IL-2, or by commercial antibodies against p24, gp41, or gp 120, and it does not inhibit the binding of antibodies against CO4, CO8, or the IL-2 receptor. Sera from some anti-HIV positive and clinically healthy individuals can neutralize the suppressive effect of the HIV-extract on lymphocyte transformation. This neutralizing effect was recovered in ammonium-precipitated immunoglobulin from the same individuals. Further investigation of antibody preparations from these sera are currently under study. (This work was supported by the Danish Cancer Society and the Danish Medical Council.)

WP.102 Serial Testing of Cell-Mediated Immunity in Haemophiliacs.

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Cell-mediated immunity (CMI) was assessed in 39 haemophiliacs by intradermal response to 7 recall antigens and compared with 20 healthy male controls. A positive response was indicated by mean diameter of induration $\geq$2mm at day 3. All control subjects were positive to 2 or more antigens and 80% responded to 4 or more. CMI was markedly depressed in the haemophiliacs with 62% responding to none or one antigen and only 18% responding to 4 or more. Eighteen anti-HIV positive patients showed no significant difference in responsiveness compared with 21 anti-HIV negative patients. However there was an inverse relationship between annual factor VIII consumption and the number of positive responses. Twenty-seven of the patients had been exposed to a single batch of factor VIII contaminated with HIV; 14 developed anti-HIV antibodies and 13 remained seronegative. Skin testing 3-9 months following exposure to this batch showed no significant difference in responsiveness between seropositive patients and those who remained seronegative. Ten patients have been re-tested 2½ years after exposure. Three symptomatic anti-HIV positive patients are now anergic (1 with AIDS, 2 with ARC) whereas 2 asymptomatic seropositive and 5 seronegative patients have maintained their cell-mediated responses.

Depressed CMI in haemophiliacs can be correlated with factor VIII usage. In the early period following exposure to HIV no difference in CMI exists between seropositive and seronegative groups. An increased prevalence of anergy is associated with symptomatic HIV infection.

WP.103 Restoration of AIDS defective Natural Killer (NK) function by OK-432

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We have recently reported that the mechanism of depressed NK activity in AIDS PBL is due to a defective "trigger-receptor" for target cell stimulation and which canbe functionally restored by IL-2 (J. Immunol. 137:1157, 1986). We have also reported that the biological response modifier OK-432 (a low virulent strain of Group A Streptococcus pyogenes), augments NK-CMC activity and secretion of NKCF by NK cells (Cellular Immunol. 102:126, 1986). These OK-432 activation events appear to be independent of IL-2 but mimic the effects of IFN and IL-2 activations of NK cells. The present study examines whether OK-432, like IL-2, can also activate AIDS NK activity. PBL from patients with AIDS/KS were treated with OK-432 for 20h, washed and tested against the NK sensitive G8 target cells in a 4h ^{51}Cr release assay. A significant enchancement of NK activity was observed which was dependent on the dose of OK-432 used. We also observed a significant enhancement of ADCC activity. These results demonstrate that OK-432 restores AIDS NK activity presumably through the same mechanism induced by IL-2. The mechanism of OK432 mediated activation of AIDS NK cells will be presented. (This work was supported in part by a grant from the AIDS Task Force, and in part by the Tumor immunology training grant CA-09120 awarded to J.D.K.)

WP.104 Detection of Antibody Dependent Cell Mediated Cytotoxicity (ADCC) Against Human Immunodeficiency Virus (HIV) Infected Cells.

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We studied the ability of serum from HIV seropositive or seronegative subjects to augment killing of HIV infected H9 cells compared to uninfected H9 cells in a 7 hour chromium release assay using peripheral blood mononuclear cells from healthy HIV uninfected donors. HIV infected H9 cells were more readily lysed than uninfected cells, supporting observations by others regarding NK activity against HIV infected cells. Much greater augmentation of killing of HIV infected H9 cells compared to uninfected cells was observed using serum from HIV infected donors.

		Target Cell			
Serum	n	H9	H9/HIV	(H9/HIV)-(H9)	
None	3	58 ± 4	66 ± 6	8 ± 3	
HIV seonegative	21	53 ± 1	59 ± 2	5 ± 1	$p < 0.001$
HIV seropositive	30	48 ± 1	76 ± 2	28 ± 2	

Optimal ADCC activity was exhibited at serum dilutions from 1:10 to 1:100, but were seen in some sera at dilutions of 1:10,000. ADCC was reduced by prior absorption of HIV seropositive serum with HIV infected H9 cells or staph protein A.

This assay demonstrates the presence of antibodies in persons infected with HIV capable of mediating ADCC in vitro. These findings may provide further insights into the immune response to HIV, and aid in the identification of immunogenic epitopes of HIV.

WP.105 Reduced Lymphocyte Cap Formation in Patients with Acquired Immunodeficiency Syndrome (AIDS) and AIDS Related Complexes (ARC)

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Isolated mononuclear cells (MNC) from 16 adult and 6 children with AIDS, 12 adults with ARC, and 12 adult controls were examined for the ability to cap (aggregation of receptor bound fluorescein conjugated Concanavalin A (Fl-Con A) to one pole of the cell). Cap formation was scored by enumerating fluorescent caps on 200 MNC. Mean %Fl-Con A caps on MNC from the AIDS or ARC patients was significantly reduced when compared to that on MNC from normal controls (27% reduction in capping in adult AIDS patients, 53% reduction in capping in the children with AIDS, and 30% reduction in capping in ARC patients, p=.001). Patchy and/or punctate fluorescent patterns were observed on the surface of MNC from the AIDS and ARC patients, while crescent shaped caps were seen on MNC from controls. Similar abnormal patterns were present when fluorescein conjugated mononclonal antibody to CD16 was used for capping on large granular lymphocytes (LGL) isolated from AIDS patients, while LGL from controls formed normal caps with anti-CD16. Normal capping was observed on MNC of 4 adult AIDS/KS patients and 2 adult ARC patients who were receiving in vivo human lymphoblastoid interferon (Wellferon) and bovine thymic peptides (Thymostimulin) therapy respectively. Two of the AIDS/KS were in complete remission. Capping of MNC correlated with the diminished responses to plant mitogens, CD4+ cells, decreased CD4/CD8 ratio, and subnormal natural killer cell cytotoxicity (expressed on a per effector cell basis) which was observed in these patients (p=.05). The consistent reduction in receptor capping on MNC seen suggests lymphocyte membrane and cytoskeletal abnormalities in patients with HIV infections which may be related to functional defects in these cells.

WP.106 Natural Killer Cell Activity Against HIV Infected U937 Cells in Homosexual Men

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Peripheral blood mononuclear leukocytes from homosexual men and heterosexual controls were tested for natural killer (NK) cell activity against HIV-infected U937 cells in a ^{51}Cr-release assay. HIV seropositive homosexual men were divided based on duration of infection: group 1, documented time after seroconversion, 12-25 mo; group 2, estimated time of infection, 27 to 43 mo. All group 1 and group 2 subjects were asymptomatic or had persistent lymphoadenopathy at the time of study. Five non-MACS patients with overt AIDS (PCP) were also studied.

Lysis of Uninfected and HIV Infected U937 Cells

Target	Heterosexual	Homosexual Male Donors			
	HIV-	HIV-	HIV+/GRP 1	HIV+/GRP 2	HIV+/AIDS
U937	39%[a]	36%	20%	19%	8%
U937+HIV	61% (8/8)[b]	41% (12/14)	34% (6/7)	24% (6/10)	7% (1/5)

[a]Mean % specific lysis (50:1, Effector:Target)

[b]Number of subjects showing greater lysis of HIV infected than uninfected U937 cells

The results show for the first time that HIV-specific natural killer cell activity can be detected in both HIV seronegative and HIV seropositive subjects and is impaired in association with longer duration of infection and presence of AIDS. This test may be useful in evaluation of efficacy of antiviral and immunomodulatory treatment of HIV infection.

WP.107 Positive Cellular Immune Responses in Humans and Chimpanzees Infected with the Human Immunodeficiency Virus (HIV).

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Only a few reports have been published describing the lack of specific cell-mediated immunity (CMI) to HIV. While this lack of CMI is understandable in patients with advanced disease, it is surprising in people that are only antibody positive without concomitant disease. We have assayed in a specific CMI assay mononuclear cells from humans that are anti-HIV positive without disease and compared them with chimpanzees that have been infected with either HTLV-III or ARV. All of the animals did not demonstrate any disease and have normal immune functions. The HIV antigens used in the assays were recombinant gp120, gp41 and p24. All 11 chimpanzees, whether they were singly or repeatedly infected, responded positively (blastogenic index > 3.0) at one or several occasions to gp120 and/or gp41 and p24. Eight of 11 anti-HIV positive humans without disease also responded to either gp120 and/or to gp41 and p24. To our knowledge this is the first report demonstrating a positive specific CMI response to recombinant HIV antigens in HIV infected humans and chimpanzees without disease. The results also suggest that the presence, magnitude or absence of specific CMI to HIV might determine the future outcome of HIV infection.

WP.108 Cytotoxic Factor Secreted by Human T-Lymphotropic Virus Type III Infected Cells

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The mechanisms responsible for depletion of T4 lymphocytes by human T-lymphotropic virus type III (HTLV-III) remain to be fully characterized. To explore the possibility that indirect effects might exist, conditioned media from HTLV-III infected cells were tested for cytotoxic cell-derived factors. The assay used measurements of cell proliferation of a murine fibroblast cell line, L929, which is sensitive to the effects of tumor necrosis factors, but non-permissive for HTLV-III replication. Significantly higher levels of cytotoxic activity were detected in peripheral blood mononuclear cell (PBM) cultures from HTLV-III infected individuals than from uninfected controls. Furthermore, PBM from an uninfected individual were found to secrete this cytotoxic activity after infection in vitro. This factor was secreted at levels ten-fold above that of the uninfected culture, 3-7 days after infection, prior to signs of cell killing and the presence of reverse transcriptase activity in the medium. Two different HTLV-I infected cell lines, Hut 102 and ATH8, were found to constitutively secrete the cytotoxic factor. Upon infection with HTLV-III, both of these cell lines manifested cell killing, but no change in the level of the secreted cytotoxic factor. Thus, the cytotoxic factor may not be a mediator of T4 lymphocyte depletion, but may be released as a result of cell killing in PBM, or as a reaction to virus replication. One must consider a role for this cytotoxic factor in several aspects of HTLV-III infection in vivo, including AIDS encephalopathy and the systemic manifestations accompanying ARC. The specific cell type synthesizing this factor, its biochemical characterization, and biological significance are being investigated.

WP.109 Immunologic Status of Patients with Chronic Progressive HIV Encephalomyelopathy (HIV-EM)

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Among a cohort of subjects across the spectrum of HIV infection, we found 41 in whom central nervous system (CNS) disease could not be explained by a definable opportunistic infection (OI). These subjects had dementia, central and cortical atrophy on CT/MRI scanning, myelopathy, and/or elevated CSF protein or leukocytes. Scans did not suggest mass lesions or multifocal leukoencephalopathy, except terminally in one case who developed CNS lymphoma. Sixteen had symptomatic CNS involvement that antedated any OI or neoplasms definitive for AIDS. Twenty-five others developed HIV-EM during established AIDS. Defects in HSV-induced cellular interferon-alpha generation in vitro and numbers of circulating helper T cells, known to be predictive of systemic opportunistic infections, were also found to be closely associated with the development of CNS-OI. Most subjects with HIV-EM had profound depression of these measures of cellular immunity, but there was more heterogeneity among the group with HIV-EM than in those with CNS-OI or systemic OI. These data suggest that HIV does not behave as an opportunistic agent for the CNS. However, they do not exclude the possibility of a role for an early HIV-specific immune defect in the pathogenesis of HIV-EM. Expression of HIV-EM may be as dependent on variant viruses and other factors as on the presence of cellular immune competence.

WP.110 Response to Vaccination in HIV Seropositive Subjects

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The serologic and immunologic responses of 21 asymptomatic HIV seropositive adults who were immunized with multiple polysaccharide, viral and protein vaccines were evaluated and compared with similarly vaccinated age, sex, and race matched HIV seronegative controls. The mean age was 24 (range 18-33) and 20/21 were male (95%). Lymphadenopathy was present in 20/21 (95%). The mean T4 count was 570/mm^3 (20% with T4 < 400/mm^3), the mean T4/T8 ratio was 0.5 (80% with T4/T8 ratio < 0.8), and 5/21 (25%) were anergic to skin tests. The number of subjects who responded to each vaccine is as follows:

Vaccine:	M	A4	A7	T	D	No response to any vaccine
HIV (N=21)	13	9	8	10	12	5
Normal (N=21)	21	15	13	9	10	0

M=Meningococcus C: response equals 4 fold bactericidal antibody titer rise. A4,A7 = Adenovirus 4, 7; response equals 4 fold neutralization antibody rise. T=Tetanus, D=Diptheria; response equals 4 fold IHA titer rise. The number of non-responders to meningococcal and adenoviral vaccines, as well as the number of non-responders to all vaccines, in the HIV group was significant ($P < 0.05$) when compared with the normals. However, the geometric mean antibody titers of HIV infected vaccine responders did not differ significantly from normals. HIV infected vaccine nonresponders did not differ from HIV infected responders in total T4, skin tests, total serum IgG, or in vitro lymphocyte stimulation assays. These data suggest that a subset of HIV positive asymptomatic subjects do not respond with antibody production to newly presented antigens; however, the majority do respond and produce functional antibody comparable to normals. At three months, no clinically apparent adverse reactions to vaccination were noted.

WP.111 Report of an AIDS Patient with Persistent Normal T Helper/Inducer (CD4) Lymphocyte Counts

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We studied a 32 year old bisexual man who has had Kaposi's sarcoma since 1983. Serial virologic studies disclose persistent HIV antibodies (by immunofluorescence and immunoblot) and HIV viremia (by culture of peripheral blood mononuclear cells). Serial CD4 lymphocyte counts (by Leu-3 cytofluorography) range from 900 to 1190 per cu mm, and CD4/CD8 lymphocyte subset ratios range from 1.2 to 1.7, all within the normal range for our laboratory. Lymphocyte responses to mitogens and natural killer cell activity were normal.

Using a panning technique, we showed that the proliferative and IL-2 responses of isolated CD4 lymphocytes to tetanus and candida antigens were impaired.

The patient's Kaposi's sarcoma lesions appear and regress spontaneously, and he is otherwise completely healthy. His wife and 2 year old daughter are also healthy and are free of HIV antibody.

The natural history of AIDS is one of progressive immune impairment characterized by a steady decline of CD4 lymphocytes. This unusual patient has had AIDS for three years and produces infectious HIV. We are encouraged by the observation that his immune function remains relatively intact, except for anergy to soluble antigens, an early lesion described by others.

WP.112 B Lymphocyte-Cytotoxic Antibodies in AIDS and Related Conditions
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Lymphocyte-reactive antibodies have been described in AIDS and ARC patients and might contribute to the pathogenesis of these disorders. While most previous reports concern presumably specific T cell-reactive autoantibodies, reactivity against normal B lymphocytes has also been found. We investigated the prevalence, strength and specificities of B lymphocyte-cytotoxic antibodies in AIDS and ARC patients as well as in asymptomatic individuals with +ve HIV serology, those considered at risk of HIV infection and controls. Sera from 6 groups of male patients/controls were studied: 1) homosexuals with AIDS and +ve HIV serology (n=16); 2) heterosexual IV drug users with AIDS and +ve HIV serology (n=10); 3) homosexuals with ARC and +ve HIV serology (n=10); 4) asymptomatic homosexuals with +ve HIV serology (n=10); 5) healthy homosexuals, -ve for HIV serology (n=15); 6) healthy heterosexuals, -ve for HIV serology (n=6). Standard microcytotoxicity assays were performed with duplicate samples on a panel of B lymphocyte-enriched (≥80%) cells from 20 normal donors, representing all well-defined HLA-DR antigens and many of the recognized HLA-A,B specificities. An average reading of "5" in the 1 to 8 scoring system for the duplicates was considered a significant cytotoxic effect.

We found a progressive increase in both the prevalence of lymphocytotoxic sera and the breadth of their reactivity in asymptomatic HIV-infected men, ARC and AIDS patients, compared with controls. For groups (1) through (6) respectively, results were as follows: (i) prevalence of +ve sera: 81.2%, 60%, 80%, 60%, 31.2% and 33%; (ii) average number of reactive cells out of the 20 in the panel: 10.8, 6.6, 6.7, 5.6, 4.6, and 3.5; (iii) average score of the +ve reactions: 7.2, 6.6, 6.7, 7.0, 5.9 and 5.5. Marked differences in reactivity within the cell panel displayed by most positive sera suggest that alloreactivity may be the underlying mechanism, but no defined patterns for either class I or II HLA specificities could be identified, and platelet absorption of 16 positive sera abolished or significantly reduced the titers of their cytotoxicity on the same B lymphocytes.

WP.113 Monoclonal Antibodies Reactive to CD4 and GP120 Block HIV Induced Fusion of Uninfected CD4$^+$ Lymphocytes
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We recently reported that mixtures of HIV infected tumor target cells (H9) and uninfected CD4$^+$ lymphocytes resulted in fusion and subsequent death of both cell types (B. Yoffe et al., PNAS in press). We have used this ^{51}Cr cytotoxicity assay to study the interaction between the CD4 molecule and the GP120 envelope protein of HIV. These proteins are thought to be responsible for the initial binding of HIV and for the development of syncytia. We used monoclonal antibodies (mAbs) reactive to the GP120 peptide 503-532 (Eur. J. Immunol. 16:1465, 1986) to block chromium release from HIV infected cells in the presence of CD4$^+$ uninfected lymphocytes. We found that mAbs reactive to the Leu3a determinant but not the OKT4 determinant on the CD4 molecule could prevent cytolysis. Two mAbs reactive to the peptide 503-532 were also shown to prevent syncytia formation and cytolysis. We also determined whether addition of anti-CD7, CD3, or Dr mAbs could block cytolysis. No effect on fusion formation and cytotoxicity was observed. These data indicate that the critical interaction involved in syncytia formation is between the CD4 molecule and a specific region on the GP120 molecule. This cytotoxicity assay is a valuable tool that may allow careful dissection of the requirements for HIV induced cytopathology.
Supported by NIH grant AI22549.

WP.114 Reduced Numbers and Increased Activation of Monocytes in Patients with AIDS.
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We analized peripheral mononuclear cells derived from 11 patients with AIDS. 12 subjects with ARC, and 10 heterosexual controls. Staining with fluorescein-conjugated LeuM3 and phycoerythrin-conjugated HLA-DR (Ia) monoclonal antibodies was carried out for immunofluorescence assay. The results indicated that in the AIDS and ARC patients there was a uniform depletion of LeuM3+ cells, or monocytes, of both the Ia- and Ia+ types. However, monocytes cultured for four days with ConA or PHA resulted a decrease in number of Ia+ cells relative to total monocytes. This observation corroborates previous reports of defects in mitogen response capabilities of antigen-presenting cells. In addition, in the fresh samples we observed an increase in the Ia-mAb binding per cell, in the Ia+ monocyte populations of the AIDS and ARC patients relative to controls. This increase of Ia-mAb binding is indicative of activation. These observations, then, refute the proposed notion that cells of the mononuclear phagocytic system in AIDS patients are deficient in Ia antigen expression. Rather, they suggest that the defects in antigen-presenting function in AIDS are due to an overall depletion of presenting cells and to impaired antigenic response. The increased activation of the AIDS monocytes may arise as an adaptive response by the cells to reduced numbers and to the antigenic overload imposed on these patients' immune systems.

WP.115 Immunological, Virological Correlates in the Clinical Progression of the Acquired Immunodeficiency Syndrome
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We have been longitudinally following a cohort of 66 control, 166 prodromal and 36 AIDS subjects for 24 months. Eight cycles of serial immunological and virological testings have been completed. All AIDS patients and 101 of 166 (69.9%) prodromal subjects were HIV(+). All heterosexual controls and 55 of 166 (30.1%) prodromal subjects were HIV(-). The following significant clinical changes have been observed: 14 of 55 (25.5%) of HIV(-) prodromals converted to HIV(+) and two of these (14.3%) further developed AIDS. Twenty-nine of 111 (26.1%) HIV(+) subjects developed AIDS, of these 11 (40.7%) died of AIDS. Of the original 36 AIDS patients 21 (58.3%) have died. Contrarwise the controls retained unchanged clinical, virological and immunological profile. Our data show that T_i; inducer T_h and regulator T_h cell subsets are significantly abnormal in HIV(-) prodromal subjects and progress to complete abrogation through AIDS and death. Lower lymphocyte function (PHA, PWM, SAC) is present in the HIV(-) prodromals, further reduction occurs at the conversion to HIV(+). Each further change in clinical status follows drastic reduction in T and B lymphocyte function. The most sensitive indicators of clinical changes are: T_h and its' subsets, SAC and PWM induced blastogenesis, CMI against auto and allo^b targets and cIgG positive cells as well as changes of anti-p17 and p24 antibodies in the sera.

WP.116 The influence of HIV infection on antibody responses to influenza vaccines
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This study was done to evaluate the effect of HIV infection on influenza vaccine responses. We studied HI antibody responses to A/Taiwan/86 (H1/N1) and A/Mississippi/85 (H3/N2) in 105 subjects 4 weeks after immunization with monovalent and trivalent vaccines containing these antigens.

Study populations included HIV -, non - risk gp. (HIV-/NR, n = 16), HIV - risk gp. (HIV-HR, n=22), HIV + asymptomatic/LAS (HIV +, Asym, n=29), ARC (n=14), AIDS (n=24). The mean age of study subjects was similar in each group. HI antibody responses (Log_2) were as follows:

	H1/N1			H3/N2		
Gp.	Pre	Post	Diff.	Pre.	Post	Diff.
HIV-, NR	2.93	8.125	5.18	2.56	7.81	5.25
HIV-, HR	4.09	8.0	3.91	3.91	7.95	4.05
HIV+, Asym	2.48	5.76	3.28	3.21	6.83	3.62
ARC	2.29	4.5	2.21	2.5	4.35	1.85
AIDS	2.88	4.21	1.33	2.79	4.38	1.58

Post vaccine antibody levels were significantly lower ($p<.05$) for HIV + Asym than HIV - NR and were lower ($p<.05$) for ARC/AIDS pts than all other groups for both H1/N1 and H3/N2. Protective levels of Ab ($\geq$1:64) were attained to H1/N1 by 95% HIV-, 48% HIV+ Asym and 29% of ARC/AIDS pts. and to H3/N_2 by 95% HIV-, 86% HIV + Asym and 29% ARC/AIDS pts. Serum levels of p24 HIV^{2}antigen did not increase significantly after immunization except in one subject.

Patients with HIV infections respond poorly to influenza immunization but showed no evidence of increased HIV replication. Additional strategies, e.g. booster doses, amantidine may be required for influenza prevention.

WP.117 Lymphocyte Phenotype and Subset Distributions in HIV Seropositive and Seronegative Gay Men Enrolled in the Multicenter Aids Cohort Study (MACS).
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Blood samples for flow cytometry studies were obtained from MACS participants in Baltimore. Based upon EL12A results for HIV antibodies, the men were divided into 3 groups: (1) Seronegative, (2) Seroconverters (within 18 months) and (3) Seropositive (persistant for at least 36 months). The distribution of lymphocyte phenotypes, subsets, and activation markers in these groups was evaluated with a 36 monoclonal antibody dual color panel. Although the CD-4 population decreased upon seroconversion, certain subsets increased: activated CD-4 cells (MAb to non-polymorphic antigen on HLA-DR) and inducers of suppression (2H4 positive). The CD-8 population expanded upon seroconversion, and certain subsets increased disproportionally: activated CD-8 cells (as in CD-4 above), and cells stained singly with 4B4 and 2H4 (many CD-8 cells stained positive for both). The number of receptors on the lymphocyte surface for DR and TQ-1/Leu-8 on both CD-4 and CD-8 cells also showed dramatic changes.

WP.118 Cellular Immune Responses in HIV Infection

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Immune alterations in functional subpopulations of T-lymphocytes have been characterized in HIV-infected individuals using in vitro tests of T-cell function and dual-color immunofluorescence analysis by flow cytometry. In contrast to the popular notion that loss of the capacity of CD4 T-lymphocytes to respond to soluble antigen is an early event after HIV infection, we found that only 10/29 individuals who had been infected with HIV for between 14 months and 6 years had evidence of depression of this functional activity. By testing the response of each person to both tetanus toxoid and Candida albicans, it was possible to distinguish generalized non-responsiveness to soluble antigens from a failure to respond to a particular antigen. Three of the men who were most profoundly deficient in the response to soluble antigen developed AIDS within 4 months. Since men with AIDS usually were deficient in this response, we propose that this T-cell dysfunction develops only as a late consequence of HIV infection. Our flow cytometric studies exclude the possibility that loss of CD4 T-lymphocyte proliferative response to soluble antigens results from selective loss of the Leu8-, 4B4+, 2H4-, or HB-11- subsets of CD4 cells. We propose that in conjunction with CD4 T-lymphocyte numbers, the lymphocyte proliferative capacity to soluble antigens is an important variable for differential staging of HIV-infected individuals. These findings have relevance for immune evaluation assessment in therapeutic interventions in AIDS.

WP.119 Amyl-Nitrite Inhalation Alters Immune Function in Normal Volunteers

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Epidemiological evidence shows an association of the incidence of Kaposi's sarcoma and nitrite use in patients with AIDS. Exposure of lymphocytes to nitrites in vitro alters cell functions. Immune function has been examined in nitrite abusers but not after nitrite exposure in humans under controlled conditions. Six HIV negative, healthy male volunteers with limited previous nitrite use, inhaled 10 doses of amyl-nitrite (0.18-0.48 ml) over 4 days(D). The subjects were drug free for several days prior to 2 baseline tests of immune function. Blood was drawn on D D, 1, 4, and 7 following inhalation. In vitro immune function tests included identification of lymphocyte subsets, natural killer cell activity, mitogenic activity to poke weed mitogen (PWM), PHA and Con A, and polyclonal induction of IgG and IgM synthesis. The pre-amyl-nitrite T4:T8 ratio was 1.56±0.21 which decreased to 1.3±0.13 immediately following inhalation. By D4 the ratio was 1.59±0.23 and the representation of T4+ cells had risen from 44.8±1.3% to 48.6±3.3%. The T8+ cells remained constant at 36.2±3.8% and 33.3±4.5% over the same time. NK cells (leu 7+) doubled between baseline levels and 2nd day post-inhalation while NK cell activity showed an initial decrease then a significant increase by D4, post-inhalation. Leu 12+ cells showed an increase from 12.6 to 17.4% between D1 and D7 which corresponded to an increase in the mitogenic response to PWM by D7. Furthermore, in vitro IgG and IgM synthesis increased 519% and 301%, respectively, between D1 and D7. Results show a nitrite-induced, non-specific immuno-stimulation which suggests that nitrites may aggravate AIDS by enhancing HIV replication or the non-specific stimulation may mask or interfere with specific immune responses to pathogens.

WP.120 Increased Levels in Plasma of Prostaglandin E_2 (PGE_2) Could Account for the Abnormalities of Cellular Immune Functions in Drug Addicts with HIV Infection.

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Recent studies have demonstrated that PGE_2 inhibit in a dose-dependent fashion a number of immunological functions and may exert a stimulatory effect on HIV replication in vitro. We have evaluated (over 2 years) the immunological, serological and clinical conditions of 201 I.V. heroin abusers (89% seropositivity), and recently we have investigated the plasma levels of PGE_2 in a group of addicts with the various manifestations of HIV infection. Plasma concentrations of bicyclic PGE_2 were determined by a radioimmunoassay (Radiochemical Centre, Amersham) in 3 groups of heroin addicts: group A (n=11) were HIV-positive, with depressed cell-mediated immunity (CMI); group B (n=10), HIV-positive with normal CMI; and group C (n=5), HIV-negative with normal CMI. The results showed a significant increase in the levels of PGE_2 in group A (436±62 pg/ml) as compared with group B (158±19 pg/ml)($p<0.001$), with group C (107±28 pg/ml)($p<0.01$) and with 7 normal controls (47±37 pg/ml)($p<0.001$). Group A, in which concentration of PGE_2 was 10 times higher than normal basal values, showed a significant reduction ($p<0.001$) in absolute numbers of T3 and T4, an inverted T4/T8 ratio, a significantly depressed response to mitogens and anergy. Furthermore, in all 26 heroin abusers studied there was a significant negative correlation between levels of PGE_2 and the following: absolute numbers of lymphocytes ($r=-0.53, p<0.05$) and of T4 cells ($r=-0.69, p<0.01$), and response to mitogens ($r=-0.74, p<0.01$). High levels of PGE_2 also correlated with clinical deterioration. Our data suggest that PGE_2 may be one of the underlying factors leading to abnormal immunoregulation and/or facilitating the progression of AIDS virus infection. To confirm this hypothesis further investigations are in progress.

WP.121 Induction of cellular receptors for Tumor Necrosis Factor by AIDS sera.

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Interferons (IFN) are capable of enhancing expression of cellular receptors for tumor necrosis factor (TNF) and act synergistically with TNF in cytotoxic and tumoricidal activities. We postulate that high levels of the unusual acid-labile IFN in AIDS patients may induce TNF receptors and sensitize TNF responsive cells in vivo. The expression of TNF receptors in tumor cells (A549, a lung carcinoma; and Hela cells) was studied using TNF-α (Genentech) labeled with ^{125}Iodine to high specificity by lactoperoxidase method. Saturation binding curves were generated with ^{125}I-TNF and the binding characteristics were analyzed to obtain receptor numbers. Serum samples from AIDS patients with high serum levels of the acid-labile IFN and cellular 2-5A synthetase enzymatic activities were used. Following treatment of the cells with AIDS sera (n=5), there was a 50 to 300% increase in TNF receptor binding as compared to that of the controls treated with normal human serum. The extent of induction of TNF receptor binding appeared to be dose-related depending on the concentration of the sera used. Similar results were obtained when cells were treated with IFN α and γ. The induction of TNF receptors by AIDS sera can be inhibited by neutralization of the sera with anti-IFN α antibodies, indicating that IFN α is the inducing agent. The receptor induction phenomenon can also be blocked by actinomycin D suggesting that synthesis of new TNF receptors might be required. Thus, these studies indicate that α IFNs in AIDS sera can induce TNF receptor expression, and may enhance the cytotoxic activities of TNF on susceptible cells. This may be one of the mechanisms involved in the destruction of lymphocytes in AIDS and thus contribute to the immunopathogenesis of the disease.

WP.122 Abnormalities of Immunoregulatory Lymphocyte Subsets in HIV Infected Subjects.

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To evaluate the relationship between the infection with HIV and immunologic abnormalities, 241 peripheral blood samples (90 positive for anti-HIV and 151 negativa) of blood donors, of politransfusad patients, of drug abusers and of subjects with ARC and AIDS were examinad. The positivity for anti-HIV was determined by commercial ELISA and confirmed by Western Blot.

Phenotype dual color cellular analyses were performed in Flow Cytometrie on FACS 440 (BD) utilizing several combinations of monoclonal antibodies.

The preliminary results showed beyond the wall known decreasa of the helper/inducer T cell and consequently tha reversal Th/Ts ratio an increase of subsets of LGL (Leu2+Leu7+) and Leu2+DR+ cells and a decrease of Leu3+Leu8+ cells.

The in vitro proliferative responses to PHA and PWM and the cutanous reactivity to 6 Recall Antigens (Multitast Merieux) wara ralated with tha changes in mononuclear cell subsets.

The T colony assay showed T cell proliferation defect in seropositive groups as to seronegativa controls.

These immunological abnormalities avident in seropositive easymptomatic subjects can occur independently of AIDS-reletad clinical aymptoms, but they may progress with time and were marked in aubjact with ARC and more marked in AIDS.

WP.123 Serum Interleukin 2 Receptor Levels in AIDS Patients

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Activation of T cells is influenced by the binding of interleukin-2 (IL2) to its membrane receptor (IL2R). IL2R is shed from the membrane of HTLV-1 infected cells, and serum levels of IL2R are elevated in renal transplant patients undergoing a rejection reaction or with CMV infections. To determine if IL2R serum levels were indicative of inflammatory, infectious or immune responses, we measured the concentration of IL2R in the sera of normal individuals, hemodialysis patients, renal transplant patients with and without evidence of graft rejection, burn patients, individuals with HIV antibody but without illness, and patiens with AIDS.

	Units/ml (mean ± SD)		Units/ml (mean ± SD)
normals	349 ± 185	thermal injury	1,750 ± 547
dialysis patients	2,848 ± 1,416	HIV+ not ill	1,361 ± 828
graft rejection	4,097 ± 1,852	AIDS patients	3,047 ± 1,580
stable transplant	654 ± 293		

In AIDS patients there was no correlation between serum IL2R concentration and the representation of peripheral blood $CD4^+$ cells, but there did appear to be a decrease in serum IL2R levels prior to death. The data demonstrates that IL2R are released into the serum in a variety of inflammatory conditions, and as such may offer a method for determining the degree of infection and clinical course of an HIV^+ individual. It is also possible that serum IL2R may block the action of IL2 on T cells and contribute to the immunodeficiency seen with HIV infections.

WP.124 Immunological cross-reactivity between HIV gp120 and a lympho-monocytic activation antigen. Distribution and modulation of the cellular protein.

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Monoclonal antibody M38 from a mouse immunized with HIV was shown to react with a protein epitope of HIV gp 120 and with a cross-reacting epitope of a cellular 80 Kd protein present on cells of the lympho-monocytic lineage (see Siccardi et al., this Congress). On sections of normal lymph nodes the antibody stains a subset of dendrite-like cells with no correspondence to known staining patterns. Fractionation of lymph node cell suspensions on Percoll gradients locates M38 positive cells in the low-density monocyte fraction; only a small percentage of this fraction, however, is stained. Peripheral blood monocytes are M38 negative and become intensely positive in plastic adherent cultures. U937 and HL60 cells are also negative but can be induced to express the 80 Kd protein by gamma interferon and other activators, as demonstrated by both immunocytochemistry and flow cytometry. In gamma interferon induced cultures of U937 the appearence of the positivity is slow and involves morphologically distinct stages, with a "late activation antigen" pattern. The involvement of the 80 Kd protein in antigen presentation is under investigation in several experimental systems.

WP.125 HIV infection of promonocytic U937 cells down regulates class-II expression, diminishes accessory cell functions and induces differentiation-like phenotypic changes

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Surface marker analysis and functional studies were performed with promonocytic U937 cells that had been infected with HIV and persistently produced virus as detected by supernatant reverse transcriptase activity. Accessory-cell function of U937/HIV cells on anti-T3 Mab- and Con A- induced T-cell proliferation was decreased to 20-60% compared to that of non-infected U937 cells. Similar accessory-cell defects were demonstrated in the monocytes of asymptomatic seropositive homosexuals, with normal CD4 T-cell numbers and ARC and AIDS patients. The accessory-cell defect could be partially restored with r-IL-2 and monocyte supernatants. Addition of $\geq 10^4$ TCID50 HIV did not affect T-cell proliferation under these culture conditions. Expression of MHC class-II antigens on U937/HIV cells was 3-10 fold decreased compared to non-infected U937 cells. HIV infection induced expression of CD11 (C3bi receptor) and p150/95 adhesion molecules and induced enhanced expression of LFA-1 α and β chains. Expression of these adhesion molecules resulted in strongly enhanced PMA-induced aggregation of U937/HIV compared to non-infected U937 cells. In addition U937/HIV cells, contrary to U937, intensely stained for cytoplasmic non-specific esterase activity. The phenotypic changes strikingly resemble the effects of differentiation-inducing agents (i.e. PMA, DMSO) on the U937 phenotype. Our results suggest that monocytes (APC) may be important target cells through which the immune system is affected by HIV.

WP.126 Comparative quantification of the C3b complement receptor (CR1) on blood cells in HIV infected patients.

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We have previously demonstrated the decreased expression of CR1 on red blood cells (RBC) of HIV infected patients, which was correlated to the severity of the HIV mediated disorders. Since the RIA employed for CR1 enumeration is delicate to perform in large scale clinical applications, we have applied to the quantification of CR1, a sensitive enhancing system for detecting low density cell surface antigens by flow-cytometry : the super-Avidin-Biotin System (SABS), using the biotinylated J3D3 anti-CR1 monoclonal antibody has allowed us to detect less than 100 sites/cell. The quantification by flow cytometry of CR1 sites on the RBC of 34 HIV positive patients and 33 negative controls was perfectly correlated (r = 0.99) with the results of the conventional RIA with J3D3. The mean numbers of CR1 sites detected by the SABS on the RBC of 17 patients with AIDS was significantly decreased (289±163) when compared with 33 normal controls (639±259, $p<0.0025$). More over, the decreased expression of CR1 on RBC was correlated to the absolute numbers of total and 14^+ lymphocytes. We have,then, investigated the expression of CR1 in neutrophils of AIDS patients. Both the antigenic (1.84×10^{-7} µmol of ^{125}I-J3D3 precipitated from detergent solubilized Neutrophils) and the functionnal expression (23 %[6-37]C3b-Rosette Forming Neutrophils[C3b-RFN]) were decreased in 14 AIDS patients when compared to normal controls (3.46×10^{-7} µmol ^{125}I-J3D3 ; 65 % C3b RFN). In conclusion : The decreased expression of the CR1 on RBC and WBC is not due to the occupation of CR1 by C3b-opsonized immune complexes because of the specificity of the J3 D3 mAb and can rather be related to the T cell immune defect.

WP.127 Generation of HIV-1-Specific Cytotoxic T Lymphocytes in a Genetically-Defined Murine Experimental System

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Cytotoxic T lymphocytes (CTL) were generated in BALB/c mice by immunization with a clone of syngeneic 3T3 fibroblasts which expresses the env gene of HIV-1 in a stable manner following transfection of the cloned env gene. These CTL are positive for the Thy-1 and Lyt-2 surface markers, and they are specific for HIV-1 antigens because they do not kill non-transfected 3T3 fibroblasts nor BALB/c tumor cells induced by murine leukemia viruses. However, the same CTL kill other mouse cells that express the HIV-1 env gene following transfection, if the target cells share class I H-2 transplantation antigens in common with BALB/c mice. The activity of these CTL is clearly restricted by the class I H-2Dd antigen of BALB/c mice, since mouse L cells doubly transfected with the H-2Dd gene and the HIV-1 env gene were recognized and killed very efficiently. In contrast, L cells doubly transfected with the H-2Kd gene from BALB/c mice and the HIV-1 env gene were poorly recognized, and low levels of killing were detected. H-2Dd antigen consequently presents HIV-1 env antigen in an optimal configuration. Moreover, class I transplantation antigens appear to modulate recognition of HIV-1 env antigen by CTL in this experimental system.

The immunogenicity and antigenicity of HIV-1 products can thus be studied under carefully controlled conditions in a murine model of cellular immunity.

WP.128 The role of virus and follicular dendritic cells in HIV-associated lymphadenopathy.

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Studies of HIV associated lymphadenopathy by histopathology and immunopathology showed conspicuous changes of follicular B-cell areas from a marked hyperplasia to complete involution. Immunohistochemistry showed a corresponding increase in follicular dendritic reticulum cells (FDRC) followed by progressive destruction of these cells during involution, concomitant with invasion of follicles by T-cells. HIV GAG antigens were predominantly associated with FDRC in hyperplastic follicles and diminished during involution. Virus replication was by in situ hybridization seen predominantly in follicles, presumably reflecting productive infection of T4 cells and/or FDRC. It was concluded that the destruction of FDRC in HIV patients is decisive for the progressive involution and dysfunction of the B-cell compartment. The appearance of follicular involution was a bad prognostic sign in follow-up studies. In vitro studies of cultured FDRC with regard to HIV-binding and productive infection substantiate the in vivo findings. Our studies indicate that HIV associated lymphadenopathy represents not only a disease of T4 cells but also of follicular antigen presenting cells (FDRC).

WP.129 Western Blot Analysis of Serial IgG, IgM, and IgA Responses to the Human Immunodeficiency Virus (HIV) in Recent Seroconverters

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The immunoglobulin (Ig) class-specific response of seroconverters to HIV infection is of potential importance to the pathogenesis of AIDS and may offer some insights regarding early detection. We used heavy chain-specific murine monoclonal antibodies at equivalent potency to identify virus-specific IgG, IgM and IgA present in 43 serial blood samples obtained at one (8 cases) or two (9 cases) six month intervals from 17 healthy men at high risk for AIDS who were part of a prospective study. Series were selected on the basis of HIV antibody reactivity by Western blot at the first bleed using a polyclonal anti-human IgG (H+L) reagent. Analysis was performed by conventional Western blot techniques using a whole virus lysate antigen and a goat anti-mouse Ig enzyme conjugate. The presence of virus-specific IgG was confirmed in all 17 volunteers. IgM was detected in 15 cases, and IgA was found in 12 cases. The IgA response was only found in cases that showed an IgM response. The IgG response was directed to all of the major gag, pol and env gene products except in one case in which antibodies to pol antigens did not appear. In contrast IgM antibodies were found to gag, pol and env proteins in 14, 12, and 9 cases respectively, and IgA responses were found in 11, 7, and 3 cases. Over time, the intensity of the IgG responses remained the same or increased in all cases, and antibodies to gag proteins appeared the earliest. The IgM and IgA responses were generally weaker than the IgG responses but showed a significant linear correlation with IgG intensity for gag and env proteins. IgM was found to persist for at least one year in 7/7 cases in which an IgM response could be followed. IgA reactivity rose over time in 10/12 cases. The pattern of development of class-specific antibodies to HIV may warrant further study.

WP.130 Cytomegalovirus (CMV) Induces Functional Abnormalities in Human Monocytes In Vitro.

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CMV, a DNA herpes virus, may cause immunosuppression and/or severe organ pathology in already immunocompromised persons. Since monocytes are a likely target of CMV, we explored monocyte-CMV interactions in vitro. Monocytes, purified by counterflow centrifugal elutriation, were inoculated at a multiplicity of infection of 1.0 with a low passaged isolate of CMV. Inoculated monocytes did not exhibit cytopathic changes or release virus. Infection was confirmed by monocyte expression of CMV viral proteins as detected by fluorescence activated cell sorter (FACS) analysis using monoclonal antibodies to immediate early, early and late CMV antigens. In addition, FACS analysis revealed that CMV-infected monocytes expressed interleukin 2 receptors and increased levels of HLA-DR, which are associated with activated or differentiated monocytes. Functionally, the infected monocytes spontaneously secreted increased amounts of the microbicidal oxygen intermediate H_2O_2. In contrast, the CMV-infected monocytes did not manifest further enhancement of phenotypic markers or functional parameters as did the uninfected monocytes following lipopolysaccharide stimulation in vitro. Moreover, infected monocytes did not support mitogen-induced T lymphocyte proliferation as effectively as control monocytes.

These data suggest that CMV infection induces suboptimal activation of monocytes which are refractory to secondary stimuli and impaired in accessory cell function. Thus, direct CMV infection of monocytes may contribute to the immunosuppression in AIDS.

WP.131 Expansion of a subset of T Lymphocytes Capable of Natural Killer Activity in Individuals Infected with the Human Immunedeficiency Virus (HIV).

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Individuals infected with the HIV are defective in natural killer (NK) activity which can be corrected in vitro by the addition of interleukin-2 (IL-2). Effectors of NK activity express the CD8 (Leu2a) as well as the HNK-1 (Leu7) antigens; T helper cells express the CD4 antigen (Leu3). We immunophenotyped the peripheral blood lymphocytes from 27 patients with AIDS and AIDS-related complex (ARC), 15 cancer patients and 18 control subjects for the expression of the Leu2a, Leu7, and Leu3. There was a significant increase in the percentage of lymphocytes coexpressing the markers Leu2a and Leu7 from patients with AIDS/ARC when compared to either cancer patients or controls ($p<0.01$). There was no difference in Leu2a+/Leu7+ expression between lymphocytes of cancer patients and controls. As expected, there was a decrease in the percentage of AIDS/ARC lymphocytes expressing the CD4 antigen as compared to controls. Furthermore, there was an inverse relationship between the expression of Leu2a+/Leu7+ and Leu3+ on cells. These data suggest that the defect in NK activity may lie in the lack of induction function that is provided by the CD4+ cells. Alternatively, it may be related to infection of the CD8+ cells by HIV. The significance of the expansion of this subset of lymphocytes in HIV infected individuals remains to be elucidated.

WP.132 Antibiotics influencing PMN-functions in HIV-AB-positives

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There is an increasing number of antibiotics which have been shown to affect neutrophil functions in healthy subjects.In HIV-positive subjects impairments of PMN-functions are known. We assessed the chemotaxis (directed migration dm:%N,index CI) and the chemiluminescence (AUC_{chem}:mV.min or $peak_{chem}$:mV) of PMNś in 10 healthy (33±8y) and 10 HIV-positive subjects (33±5y). In addition, these parameters were determined 10 h after oral intake of 1.0g ciprofloxacin (0.5g) and 1.0g erythromycin (1.0g) in HIV-positive(and healthy)subjects. Chemotaxis was performed by the under-agarose-method,chemiluminescence was measured with a LKB-luminometer after PMN-stimulation with AB-serum-opsonized S.aureus. No differences could be seen between healthy and HIV-positive subjects (dm 101 ± 19 %N,CI .69 vs. .71,$peak_{chem}$ 101±47 %N). 10 h after ciprofloxacin intake no change in the parameters could be seen in HIV-positives (dm 102±17 %N,$peak_{chem}$ 225±104mV vs. 199±93mV) and healthy subjects ($peak_{chem}$ 252mV vs. 245mV).Erythromycin reduced AUC (3.4±1.5 vs. 1.6±1.5mV,p 0.01)and $peak_{chem}$ (263mV vs. 183mV) in HIV-positives, but not in healthy subjects ($peak_{chem}$ 292mV vs. 298mV).
These data indicate no mayor differences in PMN- functions tested between HIV-positives and healthy volunteers prior to antibiotic intake. After ingestion PMNś of HIV- positive subjects seem to be more susceptible to erythromycin- interaction than cells from healthy volunteers, whereas ciprofloxacin doesn't reveal any influence on PMN- chemotaxis and -chemiluminescence.

WP.133 Aids and Autoimmunity - Mutually Exclusive Entities?

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Observation of AIDS and ARDS patients since 1981 has confirmed a striking absence of autoimmune and connective tissue diseases (CTD) with the recent exception of a reactive type arthritis in a very small number of patients. This absence of the usual autoimmune serologic reactions has been well documented in our ongoing cooperative study of AIDS patients at two University Medical Centers. To the present, 292 patients have been evaluated for autoimmune responses. The following tests have been performed: 1) IgM rheumatoid factor by latex and sensitized sheep cell agglutination (SSCAT) tests, the SSCAT being performed on the latex + sera; 2) antinuclear and organ antibodies by indirect immunofluorescence (FANA); 3) radioimmunoassays for DNAss and RNAss (Poly A) antibodies. These patients were all capable of producing antibody as shown by HIV positive titers in all and antibodies to sperm/seminal plasma in 35%. The results are:

ASSAY	UCMC (% +)	NYU (% +)	TOTAL (% +)
Latex	5/66 (8)	28/226 (12)	33/292 (11)
SSCAT	0/5 (0)	0/28 (0)	0/33 (0)
FANA	5/58 (0)	0/24 (0)	0/82 (0)

Assay controls included 17 hemophiliac and 25 normal sex/age range matched sera; only one showed a postive latex test. DNAss binding was negative; RNAss binding was significant in some of 55 AIDS sera compared to controls ($P = <0.05$). None have shown clinical evidence of an autoimmune or CTD except for 2 with a reactive type arthritis. This data has implications for the pathogenesis of reactive arthritis and also suggests that communication between immunocompetent cells may be interrupted at a very specific level.

WP.134 LYMPHOCYTE PROLIFERATION AND GAMMA INTERFERON PRODUCTION IN PATIENTS WITH HIV INFECTION.

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The capacity of peripheral blood mononuclear cells (MNC) from patients with HIV infection of proliferating and producing Gamma interferon (gamma IFN) in response to the mitogen Concanavalin A (ConA) and the antigens T.gondii, C. albicans and tetanus toxoid was evaluated. The patients were classified according to the Walter Reed staging criteria (WR). A control group of healthy individuals matched for sex and age was also included. For each patient were evaluated the number of positive responses/the total number of mitogen and antigens tested, as well as the "cpm score" i.e. the total cpm/the number of mitogen and antigens tested. The presence of Gamma IFN in the culture supernatants was assayed by a commercial RIA method and expressed in mU/ml. The mitogen-or antigen-induced proliferative response of MNC from the 8 patients in WR2 stage (LAS), as well as the production of GammaIFN in the culture supernatants, were not significantly different from those detected in the control group. In the patients in WR6 staging (AIDS) the proliferative response to antigens was absent in 6/8 and the response to ConA in 5/8. Also the mean production of Gamma IFN was significantly impaired in comparison with that observed in LAS patients and in the control group ($P<0.01$). These data which confirm previous findings in literature suggest that the impairment of T cell function occurs in the final stages of the evolution of HIV infection.

WP.135 Monoclonal anti-C1q binding immune complexes and hypocomplementemia in AIDS

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Fifteen randomly chosen AIDS patients admitted to this institution were studied for hypocomplementemia and circulating immune complex(CIC) concentrations. CIC's were measured by employing a monoclonal antibody with specificity for (CIC bound)C1q in a microtiter well ELISA assay. CIC concentrations were elevated in 7 patients(39-180 mcg/ml AHG equivalents:normal less than 34). C4 was decreased in 2 patients(8-19 mg/dl:normal 20-50), and 6 patients had low C3(35-42 mg/dl:normal 55-120). Hypergammaglobulinemia as assessed by serum IgG(IgG) determinations was present in 9 patients(1840-3600 mg/dl:normal 800-1800) while one patient had a low IgG(600 mg/dl).

There was no statistical correlation between either IgG or complement concentrations and CIC concentrations. However the 2 largest CIC increases were seen in 2 patients with IgG above 3000 mg/dl. Relationships between the type of infection and the presence of CIC increases were not found.

These studies suggest that in AIDS C1q binding CIC's are common and are not necessarily associated with hypocomplementemia which is also common. Furthermore, artifactually elevated CIC values from polyclonal hypergammaglobulinemia alone do not account for these findings. The presence of CIC's and reticuloendothelial dysfunction may play a role in the susceptibility AIDS patients have to bacterial co-infections.

WP.136 HIV Seroprevalence among Patients Hospitalized with Neuropsychiatric Illnesses in Kinshasa, Zaire.

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Numerous neurologic complications associated with HIV infection have been described. However the importance of such complications among African HIV infected patients is unknown.

To further define the clinical spectrum of HIV infection in Africa during the period April 1 to 14, 1985, an HIV seroprevalence study was performed among patients hospitalized in a center for neuropsychiatric illnesses. Ten (6.1%) of the 163 patients were HIV(+). This prevalence rate is similar to that observed in the healthy adult population of Kinshasa. Patients with the following neuro-psychiatric diagnoses were HIV(+): cerebral mass lesion 2/6 (33%), depression 3/13 (23%), psychotic delirium 2/16 (12%), hysteria 1/6 (17%), unclassifiable neuro-psychiatric illness 2/19 (11%). All 3 HIV(+) patients with "depression" presented with chronic cognitive impairement and important behavioral disturbances. In 2 of these patients with "depression" no other HIV associated symptoms or signs were found.

Our study suggests that HIV encephalopathy in Zaire may be responsible for only a minority of all neuropsychiatric diseases.

WP.137 Prognostic Significance of T4 Counts and Serum IgD Levels in a Cohort of Haemophiliacs Seropositive for Anti-HIV.

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In November 1986, amongst 300 patients regularly attending the RFH Haemophilia Centre, 106/245 (43%) of patients with haemophilia A and 1/55 (2%) of patients with haemophilia B were seropositive for anti-HIV. A cohort of 74 seropositive patients, whose dates of seroconversion are known by retrospective testing of stored serum samples, have been followed for a median period of 4.8 yrs (range 1.5 - 7 yrs). 16 (22%) of these patients have developed HIV-related illnesses, including PGL, ARC, and pneumococcal and zoster pneumonia. Only 3 patients, seropositive for 6.3, 4.3 and 3 yrs, respectively, have developed full blown AIDS. Of the 17 patients in the cohort who have been seropositive for more than 6 yrs, 6 patients (35%) currently have T4 counts below 0.4 x 10^9/l, of whom one has PGL, one ARC, and one AIDS. The 11 patients with higher T4 counts remain clinically well. Serum IgD levels were raised in patients with PGL and ARC, but showed a marked fall with T4 counts in patients who deteriorated clinically and developed AIDS. Serial T4 and IgD estimations appear useful prognostic indicators in seropositive patients. The rate of progression to AIDS seems less in haemophiliacs than in other groups at increased risk of HIV infection, but the onset of AIDS may be delayed for at least 6 years after seroconversion.

WP.138 Benign CMV-Mononucleosis in Non AIDS HIV-Infected Patients

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Benign cytomegalovirus mononucleosis (CMV-M) is a well known syndrome in normal adults. The clinical and virological features of a similar syndrome observed in 8 non AIDS HIV-infected patients (pts), and the relation with the course of HIV infection were analyzed. They were 6 men (5 homosexual), one woman sexual partner of an HIV-infected man, and one Zairian child whose mother had AIDS.

All pts had a benign syndrome with fever (n=7), transient splenomegaly (n=2) or hepatomegaly (n=1), and mononucleosis with atypical lymphocytes. Serum transaminase levels were increased in 3/8 pts. Heterophile agglutinin test was negative in 8/8 pts. All pts had either positive CMV viremia (3/7) or a 4-fold rise of antiCMV antibodies (Ab) (6/8), or both. IgM Ab were detected in 5/7 pts. The features resolved spontaneously in all pts. At the time of CMV-M, all the pts had HIV-Ab ; 5/8 had ARC and 3 were HIV asymptomatic.

In January 1987, 3/8 pts were in the same status of HIV infection as at the time of CMV-M : two ARC, one HIV asymptomatic, with a mean duration of follow-up of 17 months since CMV-M.

AIDS developed in 5/8 pts with a mean delay of 12.4 months (range 5-19) after CMV-M ; in January 1987, one was still alive and 4/5 AIDS pts had died, death occurring 4.5 months (range 2-7) after the first symptoms of AIDS ; disseminated CMV disease with extensive organ involvement was noted in 3/4 dead pts.

These features show that a benign CMV-M without severe localization (1) may occur in non AIDS HIV-infected pts, (2) might be a predictive factor of poor outcome of HIV infections as shown for high CMV Ab titer, and (3) may precede the clinical manifestations of HIV infection, thus requiring to look for HIV Ab in all pts with a benign CMV-M.

WP.139 Peripheral Neuropathy in the Acquired Immunodeficiency Syndrome: S.M. DE LA MONTE, D.H. GABUZDA, D.D. HO, R.B. BROWN, E. T. HEDLEY-WHYTE, M.S. HIRSCH. Massachusetts General Hospital, Harvard Medical School, Boston, MA. USA.

A multidisciplinary approach to study peripheral neuropathy in 21 patients with AIDS or AIDS-related complex (ARC) disclosed 11 (52%) with symptomatic neuropathies with painful dysesthesias or numbness and paresthesias (48%), weakness (33%), or autonomic dysfunction (10%). These deficits were confirmed by neurologic exam in 8 of 9 tested, and electrophysiologically using nerve conduction, late response, and electromyographic studies in 5 of 6 tested. Electrophysiologic studies demonstrated deficits predominantly in distal peripheral nerve function due to demyelination or axonopathy. Biopsy or postmortem peripheral nerve specimens from 19 of 20 (95%) patients disclosed moderate or severe demyelination (79%), axonopathy (36%), and inflammation (37%) in both AIDS and ARC patients. The concordance between the electrophysiologic and histopathologic interpretations of the nature of peripheral neuropathy was variable (0-50%) due to the low sensitivity of electrophysio-logic detection of axonopathy. Human immunodeficiency virus (HIV) was cultured from the peripheral nerves in 3 patients, but HIV antigen was not detected by immunohistochemical staining of 8 cases. The findings demonstrate that peripheral neuropathy in patients with AIDS or ARC is common but frequently asymptomatic; HIV infection in nerve is implicated as a likely pathogenetic mechanism of this syndrome.

WP.140 Effect of Corticosteroids on Immediate Survival from Pneumocystis Carinii Pneumonia (PCP) in Patients with Acquired Immunodeficiency Syndrome (AIDS).

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Retrospective review revealed 42 patients with AIDS and PCP divided into 3 groups: Group I - $P_aO_2 \geq 60$ on room air treated with antibiotics (N=17), Group II - $P_aO_2 \leq 60$ on room air treated with antibiotics (N=16), Group III - $P_aO_2 \leq 60$ on room air treated with antibiotics and corticosteroids (N=9). Compared to Groups II and III, Group I had significantly fewer patients requiring intubation, fewer ICU days, and lower A-a gradient on admission. Overall mortality of Group I (12%) was significantly lower than Group II (37.5%) but not Group III (22%). Group III had significantly longer hospitalizations and antibiotic courses than Group I. The only difference between Group II and III was significantly more patients in Group III (7/9) were treated with a combination of trimethaprim-sulfamethoxazole and Pentamidine compared to Group II (3/13). Certain patients in each group had increasing A-a gradients despite antibiotic therapy. Mortality in these sub-groups was 1/1 (Group I), 2/4 (Group II), and 1/7 (Group III). Severe PCP treated with antibiotics and corticosteroids has an overall mortality similar to less severe disease while severe PCP treated with an antibiotic alone had a higher mortality. Evaluation of combination antibiotic therapy in severe PCP may be warranted. A placebo controlled, double-blind prospective study on the use of corticosteroids in severe PCP is indicated.

WP.141 Clinical Features of Respiratory Synctial Virus Infection in Human Immunodeficiency Virus Infected Children.

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Respiratory syncytial virus infection may be severe in immune compromised hosts. We have cared for 7 HIV infected children with RSV infection, proven by RSV antigen capture ELISA or IFA. The ages of patients were 3M,6M,7M,2 yrs,3yrs, & 4 yrs. Fever > 39°C was observed in 4/7 patients. Cough & or rhinorrhea were present in 6/7 (85.7%) patients. Tachypnea was seen in 3/7 patients. Wheezing was noted in only 1 patient; a 3 yr old child who was known to have recurrent wheezing episodes in the past. Pulmonary infiltrates were seen on Roentgenographic examination of 4/7 (57%) patients. Hypoxia & respiratory distress developed soon after admission in 2 patients. One required 0.5 FiO_2 with CPAP of 5 cm of H_2O & the other 0.35 FiO_2 & ventillatory support for hypercarbia. Oxygen requirement remained unchanged despite ribavirin aerosol therapy. On the 8th day of hospitalization P. carinii & P.aeroginosa were detected in the tracheal lavage specimens of one patient. On the 11th day of hospitalization, P.aeroginosa was isolated from endotracheal secretions of the other patient and it was also isolated from the lung tissue postmorten. Both these patients died despite appropriate antibacterial,antiviral & antiprotozoan treatment. We treated HIV infected patients below 2 yrs with Ribavirin & the 2 patients above 2 yrs of age were not treated. Mortality in the<1 yr age group was 50%.

The majority of our patients presented with prolonged high fever & pneumonia, instead of bronchiolitis.

RSV may have been a contributing factor in the death of 2 patients, either directly producing respiratory distress, or predisposing to the emergence of other pathogens. Therefore in the HIV infected patients with RSV infection efforts should be made to detect other pathogenic organisms.

WP.142 Discordant Western Blot Analysis for Antibody to Human Immunodeficiency Virus (HIV) among Mother-Infant Pairs at Birth.

THE NEW YORK COLLABORATIVE STUDY GROUP FOR VERTICAL TRANSMISSION OF HIV (KEITH KRASINSKI*, *NYU-Bellevue Hospital Center, New York, NY.)

Diagnosis of HIV infection in the first year of life is confounded by passive transplacental passage of maternal antibody. There have been 43 newborn infants enrolled in the NYC collaborative study. Antibody to HIV, as measured by ELISA with western blot (WB) confirmation, is present in 24/43 (56%). We compared the WB banding patterns of serum obtained at the time of delivery for the 24 mother-infant pairs. Discordance of WB bands was present in 7 pairs. There were 4 mothers with antibody to p18 whose infants did not demonstrate anti-p18 antibody, and 3 mothers without demonstrable antibody to p18 whose infants did have antibody to p18. Five of the mothers are apparently well, one (anti-p18 pos) has rectal bleeding, and one (anti-p18 pos) has a history of prior Pneumocystis carinii pneumonia. Of 4 anti-p18 negative infants 3 have symptomatic disease possibly related to HIV infection: 1 (age 8 months) with lymphadenopathy, recurrent pneumonia and meningitis, 1 (age 8 months) with lymphadenopathy, recurrent otitis media and thrush, and 1 (age 3 months) with lymphadenopathy diarrhea and poor weight gain. One anti-p18 negative infant is well at 4 months. Two anti-p18 positive infants (age 5 and 7 months) are well, one other infant without lymphadenopathy is neurologically abnormal.

These data demonstrate that de novo production of fetal antibody to p18 occurs and can be detected when anti-p18 is absent from the mother. Negative anti-p18 status in infants could result from HIV infection depressing humoral immunity or immune complex formation with antibody of maternal or fetal origin. There are 6 symptomatic children among 24 HIV antibody positives; 4 with discordant bands and 2 with concordant maternal-infant absence of anti-p18; 5/6 are anti-p18 negtive. These preliminary data also suggest that absence of antibody to p18 at birth could be an early indicator of progressive illness.

WP.143 Microbiologic Evaluation of AIDS Virus Associated Periodontitis.

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We have recently described a periodontal disease associated with HIV infection which we refer to as AIDS-virus associated periodontitis (AVAP). It remains unclear whether this opportunistic infection is caused by organisms not commonly colonizing the oral cavity, or by the indigenous flora overwhelming the compromised host. This study was designed to investigate the microbiota associated with AVAP. Complete medical and dental histories and full mouth radiographs were obtained on 20 patients presenting with AVAP. Oral and periodontal examinations were done at the initial exam and every four weeks. Subgingival plaque samples (total of 46 sites) were collected with three sterile paper points placed to the depth of the pocket for 10 seconds. The points were immediately transferred to 0.25 ml of reduced transport fluid without EDTA and analyzed by culturing for selected periodontal pathogens and Candida. We also cultured subgingival plaque and mucosal tissues for enteric organisms, Spirochetes, and motile organisms, as well as Candida by direct microscopic evaluation. We detected Bacteroides gingivalis, B. intermedius and Actinobacillus actinomycetemcomitans in large numbers and Fusobacteria nucleatum was identified in over 75% of diseased sites, but the association between these organisms and the progression of AVAP remains inconclusive. At the most acute stages, Spirochetes and motile rods constituted greater than 50% of the organisms observed. Also, unusual protozoans were detected in 12 sites. The relationship of Candida to the pathogenesis of AVAP remains unclear, but is consistent with the invasive potential of Candida in other tissues in these patients. Preliminary data suggest that the AVAP lesion is associated with organisms typically associated with periodontal disease overwhelming the compromised host and that Candida may play a role in the pathogenesis of the disease. Investigations are in progress to identify any unusual periodontal organisms or organisms not commonly found in the oral cavity.

WP.144 Periodontal Disease in HIV-infected Male Homosexuals.

J.R. Winkler, M. Grassi, P.A. Murray. School of Dentistry, University of California, San Francisco, CA, USA.

Early detection of HIV infection is of great value in slowing the epidemic spread of AIDS, as well as providing earlier treatment of opportunistic infections associated with the disease. Oral lesions, such as hairy leukoplakia and candidiasis, are now among the first clinical signs of HIV infection. This study presents evidence that an atypical gingivitis (ATYP) and a rapidly progressive periodontal disease (AVAP) may serve as even earlier indicators. ATYP, is a gingivitis associated with a generalized inflammation of the oral mucosa and does not appear to respond to conventional therapy. AVAP is a rapidly progressive form of periodontal disease often associated with significant pain, bleeding, and extremely rapid loss of periodontal bone. Recently, we have observed in a number of patients, that the AVAP lesion has progressed into a potentially life threatening noma-like lesion resulting in the sequestration of large pieces of periodontal bone. The purpose of this study was to evaluate if these diseases have any diagnostic value of HIV infection and their relationship to other HIV-related diseases. The patient population studied was 112 patients. Less than 25% of the patients that presented for treatment with ATYP were aware of being sero-positive and less than 20% of these same patients had any other obvious signs or symptoms. On the other hand, 100% of the AVAP patients were aware of being seropositive and/or had other signs of HIV infection. Hairy leukoplakia and candidiasis were frequently associated with AVAP, 78% and 95% respectively, but not as frequently for ATYP which was 20% and 37% respectively. Interestingly, the relationship to T4/T8 ratios was quite significant. ATYP patients had ratios greater than 1 ($p<0.001$) and AVAP patients had ratios below 1 ($p<0.001$). Our data suggests that AVAP and ATYP are intraoral diseases related to HIV infection and may have predictive value in identifying HIV-infected individuals. ATYP appears to be a very early sign of HIV infection and frequently appears in the absence of other HIV associated signs and symtoms. AVAP appears to be associated with decreased T4/T8 ratios and may manifest in a potentially life threatening noma-like disease. NIH Grant-R23DE07245.

WP.145 Detection of HIV Core Antigen in the Cerebrospinal Fluid (CSF) in Patients within the AIDS Spectrum

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Patients infected with HIV often develop central nervous aystem (CNS) disorders including meningitis and progressive dementia. We have studied 20 patients (all HIV antibody positive) from within the AIDS spectrum, including 10 with encephalopathies, 8 with meningitis (4 cryptococcal, 4 viral), and 2 with polymyositis, for the presence of HIV p25 antigen in their CSF. To detect antigen, an assay was developed using monoclonal anti-p25 antibody for capture and a polyclonal antiserum directly labeled with HRP as signal. This assay is sensitive to at least 10 pg HIV/assay using a preparation of inactivated whole virus. The CSF samples were tested in a double blind manner. Subsequent data analyses revealed that 10/10 patients with encephalopathies were scored as positive using our antigen capture assay, whereas 0/10 patients with meningitis or polymyositis were positive. The average OD value for the encephalopathic patients was 0.128 ± 0.097 compared with an average OD value of 0.017 ± 0.008 for the meningitis/polymyositis group (p 0.01). In 10 of these cases where serum samples were also available, presence of antigen in CSF did not correlate with the presence of antigen in serum. These data support the conclusion that the AIDS dementia complex is related to the presence of p25 viral antigen in the CSF.

WP.146 ABSENCE OF ANTIBODIES TO HIV CORE PROTEIN CORRELATES WITH THE DEVELOPMENT OF SYMPTOMATIC ILLNESS IN PATIENTS AT RISK TO DEVELOP AIDS

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Approximately 500 sera from individuals at high risk to develop AIDS were tested by a sensitive immunoblot (western blot) assay for antibodies to the Human Immune Deficiency Virus (HIV). Selection of sera was based on their positivity by the enzyme-linked-immunosorbant assay (ELISA). Our results demonstrated that while all sera reacted strongly with the envelope gp41 protein, reactions to the core protein (p24), varied significantly among symptomatic patients. Comparison of the immunoblot banding patters with clinical symptoms of these patients indicated that about 33% of patients with AIDS-related diseases did not show any antibody reaction to the core protein (p24) and about one third of the patients' sera showed extremely weak reactions with the HIV-p24 antigen. These data are consistent with our earlier reports (Rasheed et al, Virology 150:1-9, 1986) and suggest the antibody patterns of the immunoblots may be used to monitor the wide spectrum of disease episodes seen during tha davelopment of AIDS.

WP.147 Response and Survival in Patients (PTs) Treated for Presumed versus Proven CNS Toxoplasmosis (TOXO).

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Twenty-eight patients with proven or suspected HIV related disease and abnormal head CT scans were treated empirically for TOXO (E). Nine biopsy proven TOXO pts with AIDS were also treated (B). Initial therapy included sulfadiazine, pyramethamine and folinic acid (Rx) for at least 2 weeks. Some PTs also received steroids or anticonvulsants. PTs who responded were continued on antimicrobials. Among E PTs, 21 responded clinically and radiologically in 2-4 weeks (E-R), 7 did not (E-NR). Of B PTs, 4 responded (B-R), 4 did not (B-NR), and 1 was biopsied here and treated elsewhere. There were no significant differences in the response rates of E and B PTs. Responders and nonresponders did not differ in the use of steroids with initial Rx. The 4 subgroups were similar in demographics and clinical presentation. One HIV Ab negative E-R PT and 1 E-NR pt whose CT was normal on review are excluded from further analysis.

Survival of responders was significantly longer than nonresponders by life table analysis (median 422 vs 67 days). Survival of E PTs was longer than B PTs (median 294 vs 90 days), but the difference was not significant. Median survival of the 20 E-R PTs was 309 days. No deaths occurred among the 4 B-R PTs, whose median follow-up was 365 days. Of the 6 E-NR PTs, one proved to have CNS lymphoma and 5 had lucencies and calcifications on CT suggestive of alternative diagnoses. Four of the responders discontinued Rx and relapsed, but improved when Rx resumed. Clindamycin replaced sulfa in 17 PTs because of toxicity.

PTs can be treated empirically for TOXO with response rates and survival comparable to biopsy proven cases. Empirically treated PTs without prompt responses, or who develop new lesions on Rx, should be biopsied in search of other treatable diseases.

WP.148 Memory Function and Motor Control in AIDS: An Evaluation of Some Neuropsychological Measures

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The AIDS dementia complex (ADC) has been characterized as having features similar to "subcortical" dementia, namely apathy, psychomotor slowing, forgetfulness, reduced mental agility and personality change. The formal neuropsychological examination should not only provide quantitation of relevant cognitive functions, but should also provide data that will be useful in the eventual subclassification of patients with ADC. To these ends, a range of neuropsychological tests of memory and motor function have been administered in the course of 100 evaluations of over 60 AIDS patients without evidence of focal intracranial disease (e.g., toxoplasmosis, lymphoma, PML) that would confound the characterization of ADC. The memory tests included the logical memory, paired associate learning and visual reproduction subtests of the Wechsler Memory Scale, the Rey Auditory Verbal Learning Test, and the Benton Visual Retention Test, while the motor tests included the finger-tapping, grooved pegboard and timed gait tests. Preliminary analyses indicate that different tests yielded different estimates of impairment rates, with poor verbal memory found in 10-25% of the evaluations and poor visual reproduction found in 25-45% of the evaluations. Similarly, motor abnormality rates ranged from 25-50%. Although nominally assessing similar functions, these tests also had different patterns of correlation with other neuropsychological tests, suggesting that, for the purpose of better defining the characteristics and natural history of ADC, detailed neuropsychological evaluation is an important complement to briefer examinations designed for large population studies.

WP.149 Neurological Complications of HIV Infection in the Absence of Significant Immunodeficiency

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Infection with the human immunodeficiency virus results in a wide spectrum of neurological disorders. Whilst some of these represent opportunistic infections or neoplasms, others likely result from direct HIV infection of the nervous system and/or immunopathogenic processes. These neurological syndromes include an acute meningoencephalitis related to seroconversion, chronic meningitis, dementia, vacuolar myelopathy and peripheral neuropathies. These have occurred in patients with AIDS or AIDS-related complex, as well as in HIV seropositive individuals who are systemically well. This report details the clinical features of 7 immunocompetent patients who developed neurological syndromes in the context of an acute febrile disorder and HIV seroconversion. In one case, however, there was no antecedent systemic illness. There appeared to be two phases: acute and subacute. In the acute phase, patients developed meningoencephalitis or meningoradiculitis, usually occurring within one to several weeks of the systemic illness. In the subacute phase there was either a focal dementia alone or in combination with optic neuritis, hemiparesis, ataxia or peripheral neuropathy. All patients tested were found to have cognitive impairment of a similar type but of differing degree. The relationship of this to the more chronic AIDS dementia complex is not yet clear. It is proposed that the pathogenesis of these acute and subacute syndromes is, at least in part, immune-mediated, although direct HIV infection of the brain likely initiates these disorders, particularly the dementia.

WP.150 Prognostic Indicators at Presentation of Kaposi's Sarcoma

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A cohort of 162 patients with Kaposi's sarcoma (KS) treated at San Francisco General Hospital (SFGH) was identified between November 1980 and March 1984. Baseline history, physical exam, and laboratory variables were analyzed for prognostic effects on survival. Follow-up in August 1986 determined date of death for 132 patients. Twenty-six were known to be alive at least until January 1986. 115 pts developed KS before any AIDS associated opportunistic infection (OI). Survival was calculated from Kaplan-Meier estimates.

Patients without OI had a median survival of 672 days compared to 306 days for those with OI before KS. Of the patients without OI sigoificant prognostic variables included: oral candidiasis, sedimentation rate (ESR), hematocrit (Hct), helper suppressor ratio (H/S), and constitutional symptoms (BSx): fever, night sweats and weight loss greater than 10 lbs. A dose response was noted for BSx with median survival of 1289, 657, 703, 382 days in patients with 0,1,2,and 3 BSx respectively. Median survival with and without candida was 649 vs 1069 days. As baseline Hct fell from >42, 38-42, 36-38, <36 median survival 1120, 848, 568,and 226 days. Similarly for ESR <15, 15-25, 25-50, >50 median survival was 1102, 672, 527, and 422 days. For H/S ratios <.3, .3-.7,>,7 median survival was 1102,1035,463. When Hct, or ESR, or H/S ratios were considered simultaneously with BSx in Cox regression, BSx were no longer statistically significant. Thus the laboratory abnormalities were more closely linked to prognosis than clinical symptoms. This stduy supports the collection of baseline routine laboratory studies to estimate prognosis of newly diagnosed AIDS KS and in selecting candidates for experimental protocols.

WP.151 Correlation of Specific Antibodies anti HTLV-III Proteins with the Clinical Status.

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The aim of this study was the analysis of the immune response to the proteins of HTLV-III in AIDS patients to determine whether the immunoreactivity correlates with the clinical status.

Among the 24 AIDS patients positive for antibodies to proteins coded by both gag and env HTLV-III genes, 15 are alive. Three of the remaining 9 patients died accidently. All the last 6 AIDS dead patients had neurologic diseases associated with the HTLV-III infection. 13 patients had antibodies directed only against the env encoded proteins and they are all dead, with the exception of one addict, who had an episode of PCP in September 1983. HTLV-III related neurologic disease was present in only 1 dead patient. Sequential serum samples of the same AIDS patient showed decreasing amounts of anti-gag antibodies and/or their disappearance in relation to disease progression or next to the exitus.

Progression of the disease seems to be associated with the presence of lower levels of anti gag-protein antibodies and later on with their disappearance. If patients survive for a relatively long period of time and develop the full blown AIDS, their antibody profile is caracterized by an unique reactivity for the gp41. Severe or unrecognized opportunistic infections, neurologic diseases or unrelated complications will shorten the survival. Moreover, clinical improvement seems to be followed up by the recovery of the immunoreactivity for the gag-encoded antigens.

WP.152 Evaluation of the Gen-Probe[TM] Rapid Diagnostic System for the Mycobacterium Avium Complex Using Isolates from Patients with the Acquired Immunodeficiency Syndrome.

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A new 20 test product, Gen-Probe[TM] Rapid System for the Mycobacterium avium complex, has been introduced using nucleic acid hybridization technology. Seventy-Eight isolates, identified by conventional methods, from an equal number of patients were analyzed according to the manufacture's specifications. The specimens included: 38 blood, 15 tissue, 2 stool, 10 Bronchial lavage, 10 bone marrow, 1 CSF, 1 urine, and 1 sputum. Of the 78 isolates, 72 were determined to be Mycobacterium avium and 5 were Mycobacterium intracellulare. The percent hybridization for 71 of the M. avium isolates showed a mean of 54 percent with a range from 44 - 67 percent. One M. avium isolate gave a 29 percent hybridization with the M. avium probe and a 9.7 percent hybridization with the M. intracellulare probe. The M. intracellulare isolates showed a mean of 54 percent hybridization with a range from 36-60 percent. One stool isolate gave low hybridization levels with each probe due to bacterial contamination. For cost considerations, isolates should be tested first with the M. avium probe; and if negative, followed by the M. intracellulare probe. From our studies, 77 of 78 M. avium complex isolates gave unambiguous results. The Gen-Probe[TM] test systems shows promise as a rapid diagnostic technique. Further studies are in progress to determine specificity and clinical relevance.

WP.153 FETAL AIDS SYNDROME: LACK OF CORRELATION WITH MATERNAL DRUG USE.

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The fetal AIDS syndrome (FAS) is a recognizable pattern of growth and craniofacial dysmorphic features that occurs in HIV-infected infants and children. Since the majority of these infants are born to women who are intravenous drug users, it is important to distinguish the features of FAS from those caused by fetal exposure to drugs. In an attempt to do this, 12 HIV-antibody positive children under the age of 2 1/2 years were examined by one of us who was blinded to the mothers' history of drug use. Using the criteria of the FAS scoring system, the subjects were divided into 3 groups: (1) severely stigmatized; (2) moderately stigmatized; (3) mildly or not stigmatized. Seven of the subjects were offspring of confirmed maternal drug users; of these, 3 were severely stigmatized, 3 were moderately stigmatized and 1 fell into the not stigmatized category. Five subjects were born to women who had become infected through heterosexual contact; 2 scored in the severely stigmatized category, 2 were judged to be moderately stigmatized and 1 was not stigmatized. When these data were analyzed, no differences in FAS score between the etiology groups could be identified. Although this study population is small, these preliminary findings suggest that FAS occurs independent of fetal drug exposure and that the features are related to infection with HIV during the first trimester of intrauterine life.

WP.154 Multifocal Cytomegalovirus Brain Infection in AIDS: Early Detection with Magnetic Resonance Imaging and Treatment with 9-(2-hydroxy-1-(hydroxymethyl)ethoxymethyl) guanine .

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A 43-year-old man with AIDS had clinical evidence of multifocal disease of the brain; however, computed tomography (CT) was negative. Magnetic resonance imaging (MRI) revealed multifocal lesions, proven to be caused by cytomegalovirus (CMV) by brain biopsy. CMV encephalitis was documented by light and electron microscopy as well as by immunohistochemical staining of the biopsy specimen. CMV viremia was confirmed by a positive urine culture. Therapy with 9-(2-hydroxy-1-(hydroxymethyl) ethoxymethyl) guanine (BW B759U) resulted in stabilization of the patient's clinical disease and radiographic improvement of the multifocal lesions.

In AIDS patients, multifocal brain lesions on CT or MRI are seldom due to CMV, but this diagnosis must be considered in the differential. MRI is currently the procedure of choice for detecting these central nervous system lesions. Early brain biopsy is warranted, since CMV encephalitis is a potentially treatable infection.

WP.155 Gestational Characterstics and Mode of Delivery of 98 Children with AIDS in New York City.

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It has been established that Human Immunodeficiency Virus (HIV) can be transmitted from infected mothers to their offspring, probably in-utero, but the possibility of intrapartum transmission has not been disproved. If it occurs, Caesarian section (CS) delivery might be protective. We examined birth certificate records of 98 children reported with maternally transmitted AIDS in New York City (NYC) born between 1977 and 1986, and all children born in NYC during the year 1983, to assess CS delivery rates and other characteristics including birthweight. Of the 98, 71 (72%) had mothers who used intravenous narcotics (IVDU). Eleven of 62 (18%) black, 5 of 26 (19%) hispanic, and one of 10 (10%) white infants with AIDS had been born by CS compared with 18% of 33,495 black, 20.5% of 31,083 hispanic and 25% of 32,787 white infants born in 1983. Differences were not statistically significant. Children who subsequently developed AIDS were more likely than the general cohort to be underweight at birth: 39% of blacks, 38% of hispanics, and 40% of whites under 2500 grams, vs. 12% of all black, 8% of all hispanic, and 4% of all white births. Of infants with AIDS born to IVDU mothers, 44% were under 2500 gms vs. 33% of 843 infants with maternal narcotics listed on the birth certificate. Further matching by sociodemographic characteristics may lessen this difference. Prospective studies comparing infected and uninfected pregnant women will further elucidate the effect of HIV on fetal growth. Since the CS rate for delivery of infants who later developed AIDS was not lower than the rate for the general cohort, our data indicate no protection from C-section delivery.

WP.156 Cerebrospinal Fluid (CSF) Findings in HIV Positive Patients (pts) without AIDS.

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Lumbar punctures were done on 114 consecutive pts. without AIDS evaluated for a positive HIV by Western blot. Fifty-seven pts. had normal CSF (grp I). Forty-four pts (38.6%) had abnormal (abnl) CSF (grp II), defined as: protein > 50 and nucleated cells (N.C.) ≥ 7; or, protein ≥ 60 alone; or, N.C.≥ 10 alone; or an elevated CSF IgG or IgG synthesis rate or the presence of oligoclonal bands (OCB). Grp III (57 pts) included all grp II pts plus 13 other pts meeting the standard criteria for abnl CSF: protein > 45 or NC > 5. No significant differences existed between grps for age, sex, race, serum FTA, Walter Reed classification, CD_4 count, or CMV, toxoplasma or EBV serologies. Grp III CSF findings revealed:27 pts with protein > 45 (range 22-104); 36 pts with > 5 NC (range 0-35); mean differential 0.3% polys, 90.7% lymphs, 9% others. Bacterial, fungal and AFB cultures were negative. Thirty-one pts in grp II (72%) had an elevated CSF IgG, IgG synthesis rate or OCB.

No significant neurologic abnormalities could definitely be attributed to these CSF findings. Head CT scans on 33 pts in grp II were abnl in 3, one of whom had an abnl MRI. This study demonstrates that significantly abnl CSF is present in about 38% of pts with HIV infections without AIDS. Follow-up of these pts will clarify the significance of these findings and their relationship to HIV CNS infection.

WP.157 A Prospective Study of Human Immunodeficiency Virus (HIV) Infection in Pregnancy.

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Between 1/15/86 and 11/15/86, 278 pregnant women, including 67 Drug Addicts (IVDA), 195 Haitians and 16 sexual partners of risk members were offered HIV testing. Seventy-seven percent (215) agreed to testing. Forty-three percent of the IVDA's (N=20), 5% of the Haitians (N=8), and 43% of the sexual partners (N=8) were confirmed seropositive. Eight women were notified of their seropositive status prior to 24 weeks of pregnancy; only one woman elected abortion. To date 57 women, (24 positive and 33 negative) have delivered. Among IVDA's 2/20 negative patients had preterm deliveries compared to 6/17 positive patients. The average birthweight among seropositive IVDA's was 2579 vs. 2899 for seronegative patients. Among Haitians, all had term deliveries with the mean birthweight 3,310 in seropositive mothers and 3,420 in seronegative. There was no significant difference in the cesarean section rate. Among positive patients two had syphillis, two had hepatitis and one had amoebiasis. Among seronegatives two had UTI's and four had parasites. All children of seropositive mothers demonstrated at least passive seropositivity at birth while no children of seronegative women had antibody. Follow-up studies of children is ongoing. Seropositivity is often found among asymptomatic parturients from risk groups and may impact on birthweights.

WP.158 Multimodality Evoked Potentials Studies In AIDS, S.M. VISHNUBHAKAT, M.KAPLAN, R.BERESFORD, B.FARBER, T.FLYNN, North Shore University Hospital, Manhasset, N.Y., U.S.A.

HIV induced central nervous system disease (CNS) has been largely studied neuroradiologically and clinically without electrophysiologic studies which may indicate pathology in asymptomatic areas of CNS. We studied 35 patients (18 homosexuals, 15 addicts, 2 others, 30 males, 5 females, 30 AIDS, and 5 AIDS related complex) with visual, auditory, and somatosensory evoked responses in order to determine incidence, pattern, and extent of central conduction abnormalities. These studies were performed using Seigen clinical averager with computer facilities. Stimuli were delivered by pattern shift television screen for visual evoked response (VER), 100 decibal clicks for brainstem auditory evoked response (BAER), median nerve stimulation for somatosensory evoked response (SSER). Thirteen patients showed abnormalities in one or two of the three modalities studied Five patients had VER and five had SSER abnormalities whereas 7 patients showed abnormalities in BAER. Five patients had VEP abnormalities, 3 had bilateral, 2 had unilateral prechiasmatic delay. None had significant visual symptoms, though visual acuity was abnormal in three. Five patients had SEP abnormalities, 3 had peripheral delay suggesting neuropathy, and 2 had cervical delays suggesting myelopathy affecting posterior columns. Seven patients showed BAER abnormalities 6 had delay involving pontine pathways, whereas one had peripheral delay suggesting auditory nerve involvement. Clinical evaluation failed to reveal significant neurologic signs indicative of the abnormality revealed by EP studies. There was no correlation between EP abnormalities and staging of AIDS. Eight of the thirteen patients showed presence of peripheral neuropathy in another study. We conclude that approximately 36% patients with AIDS will reveal abnormalities in multimodality evoked response study and indicate presence of CNS pathway abnormalities in largely asymptomatic areas.

WP.159 Clinical and Electrophysiological Features of Neuropathy in AIDS

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Peripheral neuropathy is a known complication of AIDS. Its incidence and electrophysiologic features have not been established fully. We studied 35 patients with sensory motor latency, amplitude, conduction velocity, and long latency determination, and electromyography. These studies were performed using TECA 4 machine with photographic recording for analysis of electroneurogram and myogram. There were 18 homosexuals, 12 addicts, 3 addict wives, 1 secondary to transfusion, and 1 with no known risk factors. Thirty-one were male and 13 were symptomatic with predominantly peripheral symptoms of tingling and numbness in 9 and focal neuropathic symptoms in 4. One patient complained of proximal weakness. Neurological evaluation confirmed features of neuropathy in 14 patients and consisted of mild distal sensory loss in 12, and mononeuropathy in 2. Twenty-eight patients had opportunistic infections from AIDS, and five were classified as suffering from AIDS related complex.

Electrophysiologic Studies: Two of the 33 patient had carpal tunnel syndrome and 3 had mononeuropathy associated with peripheral neuropathy. Eighteen patients had symmetric peripheral sensory motor neuropathy without any evidence of either proximal neuropathy or radiculopathy. Seven of these patients showed mild to moderate distal sensory neuropathy and 11 had mixed distal sensory motor neuropathy. No instance of pure motor neuropathy was seen. Three of the 18 patients showed features of axonal neuropathy, whereas 15 had mixed features of both axonal and demyelinating type. One of the 10 patients who had normal electroneurography revealed EMG evidence of proximal myopathy.

We conclude that careful EP studies will reveal significantly higher incidence of peripheral neuropathy in AIDS and related complex than currently believed. We postulate variable etiologic factors based on the above studies.

WP.160 Pituitary gland involvement in AIDS : a 57-case pathological study.

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Autopsy reports in 128 cases of AIDS were examined. Fifty-seven cases included a pathological study of the pituitary gland. In 44 of them (77%) no lesion was found. In 13 cases (23%) major lesions were present : 9 infections and 4 vascular anomalies. Among the 9 infections, 5 were due to cytomegalovirus (CMV), 2 to cryptococcus sp., 1 to toxoplasma gondii, 1 to M. tuberculosis. Vascular anomalies were coagulation and ischemic necrosis (2) or micro-thrombosis of the neuro-hypophysis vessels (2).

The 5 patients with CMV had disseminated infection ($\geq$ 3 organs), conversely in 20 patients with disseminated CMV infection 1S had a normal pituitary gland. Both patients with cryptococcal infection of pituitary gland also had meningeal and disseminated crytptococcosis. Patients with tuberculosis and toxoplasmosis of pituitary gland also had cerebral and disseminated disease. All patients had multiple opportunistic infections involving organs other than pituitary gland ($\geq$ 2). Signs and symptoms of hypophyseal dysfunction were not noted due to the end-stage clinical status.

These findings suggest that hypophyseal function has to be investigated carefully at an earlier stage of AIDS.

WP.161 HIV Infection: Unusual Viral Necrotic Skin Lesions

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Herpetic virus skin lesions can often have peculiar clinical aspects in AIDS patients because of immunedeficiency: chronic perianal ulcerative Herpes simplex, maculo-papular or vescico-bullous Cytomegalo-virus lesions have been described.

In September 1986, 2 young males were admitted to our department, the first suffering from condylomata, the second from Kaposi's Sarcoma and Oisseminated Molluscum Contagiosum. They were both HIV infected and they had already suffered from Pneumocystis carinii pneumonia in 1986. We were striken by some unusual cutaneous necrotic lesions on the trunk and limbs of both patients.

The lesions were few (about 10 per patient), 4-10mm in diameter, monomorphous, not-painful, round-shaped. The centre of the lesions was filled with a dark crust. Only some of them showed a slightly elevated erithemato-vescicular border. At histological examination the epidermis and the dermis were necrotic and a multilocular vescicle with some degenerating balloon cells was seen at the border of the central necrotic area.

A herpes virus family infection was suspected and ultrastructural, cultural and immunohistochemical examinations were performed. Culture was negative but at the electron microscopy numerous viral particles, approximately 100 nanometers in diameter, with a icosahedral nucleocapside were seen in the higher layer of epidermis both in the nucleus and in the cytoplasm of keratinocytes. Both patients were treated by intravenous aciclovir with only a slight and transitory improvement of the lesions. We think that this kind of lesion could be a new expression of a herpetic virus cutaneous disease.

WP.162 Correlation between Number of T-helper (Th) Cells, Lymphocyte Response to Pokeweed Mitogen (PWM) and HIV Antigenemia in Seropositive Homosexual Males

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During the clinical deterioration of HIV infected persons from a healthy carrier state to AIDS, the number of T-helper cells as well as the lymphocyte response to mitogens frequently declines. Further, it has recently been observed that HIV antigenemia is more frequent among HIV infected individuals with symptoms than those without symptoms. In order to test the possible connection between HIV antigenemia and abnormal immunological parameters, irrespective of the clinical condition, we used a sandwich ELISA to test for HIV antigenemia in 160 seropositive homosexual males with and without immunological abnormalities.

Serum and lymphocytes were drawn at the same occasion. The investigated subjects were separated in 4 groups, comprising 1) 40 persons with Th-cells >500/µL and PWM-response > 20% of normal controls, 2) 40 with Th-cells >500/µL and PWM-response <20%, 3) 40 with Th-cells <500/µL and PWM-response >20%, and 4) 40 with Th-cells <500/µL and PWM-response <20%.

The prevalences of HIV antigenemia found were in group 1) 5%, group 2) 5%, group 3) 13%, and group 4) 23%. The differences between group 1 and 4 were statistically significant ($p<0.05$). Thus, it seems as if the presence of circulating HIV antigen is associated rather with the viral induced decay of Th-cells than with the functional capabilities of these.

WP.163 Observations following Splenectomy for HIV Associated ITP

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Immune Thrombocytopenic Purpura (ITP) is a major hematologic abnormality among hemophiliacs infected with the human immunodeficiency virus (HIV). Splenectomy is known to have a long lasting beneficial effect on resolving ITP but has been associated with an increased incidence of bacterial sepsis.

To determine the effect of splenectomy on the immune system of hemophiliacs, 10 splenectomized hemophiliacs were studied, (6 before and sequentially after surgery for up to 5 years.) All patients had some findings directly related to HIV infection ie. fever, fatigue, night sweats, weight loss and generalized lymphadenopathy which resolved following splenectomy. Concurrent to this sustained clinical improvement we noted a dramatic increase in platelets, lymphocytes and T cells.

n = 6 (10^9/L)	Pre-Splenectomy (mean ± SD)	Post-Splenectomy months postoperatively 6	12	18
Platelets	38±11	383±96	323±34	419±149
Total Lymphocytes	2.83±2.77	5.39±2.24	5.96±1.39	4.98±1.09
Leu 2 (Suppressors)	.38±.23	2.72±2.19	2.27±1.25	2.11±.86
Leu 3 (Helpers)	.43±.12	.93±.3	1.44±.35	1.24±.54
Leu 4 (Total T cells)	.67±.26	3.29±1.53	3.86±1.27	3.55±.75

One patient died suddenly 3 years after splenectomy from pneumococcal sepsis. We conclude that splenectomy in this group is an effective treatment of HIV related ITP. Although it is associated with a risk of overwhelming sepsis an overall improvement in clinical status with respect to HIV is also noted. The importance of the sustained increase in T cells and relationship to possible changes in immune function remains to be determined.

WP.164 Aerosol and gallium scans in HIV infected patients with normal chest X-rays and pneumocystis carinii pneumonia.

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In 60 HIV infected patients suspected of pneumocystis carinii pneumonia (PCP), we performed graded gallium scans and measurements of alveolar permeability with 99mTcOTPA aerosol clearance before the bronchoalveolar lavage (BAL). Nineteen patients had proven PCP and were non smoking and non drug addicted. They were selected for this study. Seven of them had normal chest X-rays. Nine had normal PaO2 (96±4.8 SD mmHg). Eleven were followed by repeated scanning after treatment. Gallium scan is positive in 13/19 patients and 99mTcDTPA clearance in 19/19 (5.41±1.7%.min-1,p 0.001 versus control 1.1±0.34%.min-1,n=10) suggesting an increase of the permeability. Gallium scan is positive in 3/7 patients with normal chest X-rays, two having hypoxemia. By contrast 99mTcDTPA scan was always positive in these 7 patients even when PaO2 is normal. Their mean clearance was 6.22±1.97%.min-1, the lower value being 3.2%.min-1 i.e. three times the normal. Under treatment, 7/11 patients normalized both tests. Four normalized gallium but not clearances : one died from extrapulmonary disease ; in the others, BAL demonstrated 1)cryptococcus, 2) pneumocystis, 3) high lymphocytosis without opportunistic infection. Gallium scan can detect PCP when chest X-rays is normal but failed in this study in 4/7 cases which were all detected by DTPA clearances measurement. This test cheaper than gallium scan is highly sensitive (100%) of PCP and normalized with recovery. Since the results are obtained in less than an hour contrasting to 48 hours for gallium scans, this test could be used to decide BAL in patients with suspected PCP, normal chest X-rays or blood gases.

WP.165 Prognostic value of laboratory parameters in the clinical course of HIV-infection

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The rate of deterioration in the clinical course and the factors for the individual prognosis of patients with HIV - infection remain to be determined. In 100 Patients Neopterin (Np), Beta-2-Microglobulin (B2), immunoglobulin (Ig), platelets (Ptl), leukocytes (WBC), lymphocytes (Ly) and the score of the skin-test (Multitest Merieux)(DCH) were measured and related to the clinical stage in the Walter Reed classification (WR). After a mean observation of 12.4 months 31% showed deterioration, 4% regression of their WR-stage. Only Np showed a significant difference between infected (WR 1) and uninfected (WR 0) persons ($p=0.01$). At the end of the follow up period a significant increase in all stages concerning Np ($p=0.005$) and Ig ($p=0.025$), respectively a decrease of DCH ($p=0.001$) was observed, in contrast to the other not significantly changed variables. Those patients who showed deterioration in the coming observation period had significantly higher Np values ($p=0.05$) and lower Ptl ($p=0.005$) in the first examination than those who remained unchanged.

So the platelet counts and Neopterin values appear to have a predictive potency for the individual prognosis of HIV-infected persons.

WP.166 Syndrome Approaches to Early and Late Outcomes in Pediatic AIDS
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A number of distinct clinical syndromes have been identified in longitudinal natural history studies of children with HIV infection. Of 142 cases of HIV infection in infants and children identified in South Florida between January 1981 and December 1986, 134 (94.3%) represent perinatal infection. The remainder acquired the infection from a blood or blood product transfusion. Of the 134 perinatal cases the overall mortality is 35%. In infants who meet the current CDC criteria for the diagnosis of AIDS, overall mortality is 74%. An analysis of survival indicates that the majority of deaths occur in the first 2 years of life and some clinical patterns are associated with an especially poor prognosis. In our series 14 infants developed Pneumocystis carinii pneumonitis in the first 12 months (mean 6) with an 86% overall mortality. Although the overall mortality rate decreases significantly after age 2 there are several late outcomes of this infection that are associated with significant morbidity and mortality. Progressive neurologic disease has occurred in 14 children in our series with a mean age of onset of 18 months (range 1-90) and an overall mortality of 57%. The development of lymphoid interstitial pneumonitis in 35 children was associated with a better prognosis. Mean age of onset was 16 mos. (range 5-35) and overall mortality was 26%. A similar mortality rate, 33% occurred in 6 children with nephrotic syndrome (mean age of onset 36 mos, range 20-61) however this syndrome has significant morbidity associated with the development of renal failure. Overall, the prognosis for children with syndromes characterized by a lymphoproliferative response to HIV (LIP and nephrotic syndrome) is better than for those with syndromes (early PCP and neurologic syndrome) associated with deficient immune responses as suggested by normal immunoglobulins, lymphopenia and a lack of lymph node enlargement.

WP.167 Nocardiosis in Patients with Human Immunodeficiency Virus (HIV) Infection
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Nocardia asteroides infection has been infrequently reported in patients with HIV infection. During a 21-month period, N.asteroides infection was documented in 10 patients with antibodies to HIV (ELISA). There were 9 men and 1 woman aged 21-38 years (mean=33.5). Eight were intravenous drug users. Only 1 had antecedent AIDS, but 7 of 7 tested had cutaneous anergy, and 8 of 8 studied had decreased T4 lymphocytes. One had concomitant Pneumocystis carinii pneumonia. N.asteroides infections included pneumonia in 5, pneumonia and chest wall abscess in 1, and localized abscess of brain (1), skin (1), retroperitoneum (1), and mediastinum (1). Mean duration of symptoms before diagnosis was 42 days (range=7-84). Seven patients were treated with sulfadiazine, 2 with trimethoprim/sulfamethoxazole, and 1 with minocycline and cycloserine. Six of 8 evaluable patients improved, but after discharge, compliance was poor and 8 patients died with clinically active disease within 2-12 months. Autopsies in 3 patients disclosed persistent N.asteroides in all; 2 had concomitant disseminated cytomegalovirus and Mycobacterium avium-intracellulare infections. One compliant patient continues to do well 5 months after diagnosis; the other has shown clinical recurrence 3 months after presentation due to noncompliance with treatment.

N.asteroides is an important opportunistic pathogen in patients with HIV infection and can precede or occur sumultaneously with other opportunistic infections. Specific antimicrobial therapy is associated with improvement but prolonged treatment appears to be necessary.

WP.168 Malaria in African Patients with AIDS
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Chronic malaria is endemic among adult natives of central Africa and represents a major cause of morbidity and mortality. Acquired immunity to malaria, believed to be predominantly humoral, is prevalent among the population of this area. We studied the clinical course and autopsy findings of two black African patients who presented with malarial infections and AIDS.

	Age	Sex	Presenting Complaints	Habitus	Exam*	Hgb	WBC
1.	37 years	M	anorexia, weight loss, cough	cachectic	HSM	8.8 g/dL	3650 mm^{-3}
2.	31 years	F	anorexia, weight loss, malaise	cachectic	HSM, DLA	8.0 g/dL	4000 mm^{-3}

* HSM = hepatosplenomegaly, DLA = diffuse lymphadenopathy

Clinical Course: Blood smears at presentation revealed malarial trophozoites in both patients (P. falciparum in patient 2). In patient 1, malarial parasites dissappeared after antimalarial therapy but fever and anemia persisted. The patient developed bilateral miliary pulmonary infiltrates and died in respiratory failure 6 weeks following presentation. Patient 2 (HIV seropositive) was treated with chloroquine and quinine but developed progressive pulmonary insufficiency and died 9 weeks following presentation.

Autopsy Findings: Patient 1: Disseminated Histoplasma capsulatum var duboisii and multifocal visceral Kaposi's sarcoma. Patient 2: Disseminated nocardiosis, intestinal cryptosporidiosis, cytomegaloviral adrenalitis, and visceral Kaposi's sarcoma. There were no malarial parasites in any organs of either patient.

Conclusion: Despite profound immunodeficiency and associated bacterial, fungal and viral infections in these patients, their chronic malarial infections were not overwhelming before antimalarial therapy, and malarial parasites were not seen at autopsy. The absence of fulminant malaria suggests that malaria may not represent an opportunistic infection in patients with AIDS.

WP.169 Polyclonal Polymorphic B-Cell Lymphoproliferative Disorder (PBLD) In Children with AIDS
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An unusual lymphoproliferative disorder occurring in 4 children with AIDS is described. All patients satisfied the criteria for pediatric AIDS reported by us (Human Pathol 1985;16:241) and had positive HTLV-III serology. Lung, spleen, kidneys, liver GI tract and lymph nodes showed gross nodular and/or microscopic infiltrates composed of lymphocytes, plasma cells and occasional immunoblasts. Cell marker studies showed preponderance of B cells. Immunoperoxidase stains for both Kappa and Lambda chains were positive in the infiltrates. Vessel wall invasion was seen in the spleen and kidneys. Cellular atypia, atypical mitosis and necrosis were absent. Two of the children had high EBV titers. We have designated this lesion as polymorphic polyclonal B cell lymphoproliferative disorder (PBLD). It may be a borderline lesion and not a full-fledged malignant neoplastic process. In pediatric AIDS systemic lymphoid hyperplasia (LH) including Pulmonary LH/Lymphoid Interstitial Pneumonitis complex reported by us (Human Pathol, 1986;17:641) and PBLD comprise the spectrum of lymphoid proliferation possibly associated with EBV. The spectrum also includes full-fledged malignant lymphoma.

WP.170 The Pathology of Pediatric AIDS: A Review of 33 Cases
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Case summaries and pathologic material from 33 pediatric patients were reviewed. Twenty-seven complete autopsies were performed. The case mix included 2 teenagers and 22 babies under 15 months of age. All patients had failure to thrive. Seventeen patients had severe thymic atrophy and 11 had lymphadenopathy. Opportunistic infections included: candidiasis, 12 cases; Pneumocystis carinii, 10 cases; and cytomegalovirum, 9 cases. Lymphocytic interstitial pneumonitis was seen in 10 patients. Adenoviral infection was documented in 3 children and 3 had E. coli sepsis. Other infections included Cryptococcus neoformans, mycoplasma, Herpes simplex, miliary M. tuberculosis and M. avium-intracellulare, B. pertussis sepsis, recurrent salmonellosis, recurrent pneumococcal meningitis of various strains, staphylococcal sepsis, and aspergillosis.

Central nervous system pathology in 14 brains included cortical atrophy, hydrocephaly, perivascular calcification, leukoencephalopathy, and proliferative vascular lesions. Gastrointestinal lesions included ulceration, villous atrophy, crypt necrosis, hyperplasia of Peyers patches, and cryptosporidial infestation. Other entities included desquamative interstitial pneumonitis, focal myocarditis, and generalized polyclonal, polymorphic B-cell proliferation.

AIDS is the commonest congenital infection in the U.S.A. In contrast to adults, infants succumb to opportunistic and common childhood pathogens . The stage of destruction of lymphoid tissue varies with the duration of illness. In AIDS and other infectious diseases of infants, the earlier the onset, the more rapid the progression.

WP.171 Impermeability of Condoms to HIV and Inactivation of HIV by the Spermacide Nonoxynol-9.
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The impermeability of condoms to HIV as well as the ability of the spermacide, nonoxynol-9 to inactivate HIV was examined. Each condom tested received a 4ml inoculum of HIV virus ($2x10^6$ reverse transcriptase units). The condom was then placed over the plunger of a 50 ml disposable syringe. To model intercourse, the plunger of the syringe was pushed up and down forcefully 50 times into the syringe. After 50 plunges, media containing H9 cells was drawn up into the syringe, making contact with the external surface of the condom. The cell suspension was then cultured. No virus was detected in the H9 cells by the cytoplasmic RNA dot blot assay or by assaying cell supernatants for reverse transcriptase activity after 12-25 days in culture.

Nonoxynol-9 was found to be cytotoxic at a dilution greater than .0005% necessitating that the nonoxynol-9 be removed from the virus by ultracentrifugation before inoculating of H9 cells. Nonoxynol-9 was found to inactivate HIV at a final concentration between .05% and .005%. Nonoxynol-9 does not interfere with reverse transcriptase activity nor does it degrade the viral RNA as indicated by dot blot. The effectiveness of nonoxynol-9 present in a condom in inactivating HIV in the case of the damaged condom was also tested. In 8 of 12 (66%) condoms, no virus was detectable 15 days after inoculating H9 cells with HIV passed through a torn nonoxynol-9 containing condom. These data suggest that condoms are impermeable to HIV and that the spermacide nonoxynol-9 can directly inactivate HIV.

WP.172 Changes Over Time in Anogenital Practices in a Cohort of Homosexual/bisexual Men

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Detailed information on sexual practices and HIV antibody status were obtained at 6-month intervals in a cohort of initially asymptomatic homosexual/bisexual men at a Boston community health center. Over 200 men have been followed for at least 12 months. At the 12-month visit, 26% of subjects who reported insertive anogenital contact (IAG) always used a condom, while 30% sometimes did. The percentages for their partners' condom use in receptive anogenital contact (RAG) were: always 32%, and sometimes 25%. Condom use was infrequent in other practices. Condoms were used more frequently by subjects with multiple partners. Between the initial and 12 month visits, the percentage of subjects reporting IAG decreased from 70% to 60%, and RAG decreased from 65% to 53%; the percentage reporting IAG who always used a condom increased from 4% to 28%, while the percentage reporting RAG who never had exposure to the partner's ejaculate increased from 18% to 45%. In spite of this encouraging trend, 31% of HIV seropositive men reported unprotected IAG with multiple partners and 16% of HIV seronegative men reported unprotected RAG with multiple partners at 12 months. Results of sociodemographic, attitudinal, and other determinants of unsafe anogenital contact will be presented.

WP.173 SEXUAL BEHAVIOUR AND CONDOM USAGE BY HOMOSEXUAL MEN IN LONDON

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This study was performed at the Department of Genito Urinary Medicine, Westminster Hospital, London between January and March 1986. Homosexual men practising ano-genital intercourse were asked to complete a questionnaire on sexual behaviour and condom usage. Approximately one third of clinic attenders practised only "safe-sex" (i.e. masturbation and body rubbing) and were excluded from the study.

Data will be presented on 145 men and examines :-

1. The association between ano-receptive and ano-insertive sexual behaviour preference and the presence of a regular sexual partner.
2. The number of sexual partners in the previous month and the presence or absence of a regular sexual partner
3. Sexual behaviour preference and condom usage
4. HIV antibody status and condom usage
5. Duration of condom usage
6. Frequency of condom splitting or bursting
7. Types of lubrication used

The 28% of men who were frequent condom users were asked to try a type of sheath promoted as being stronger than those presently available. A spermicidal gel containing nonoxynol-9 was also given as a lubricant. Data examining their acceptability and possible advantages will be presented.

This study is being repeated during 1987 in order to assess changes in sexual behaviour, with particular reference to condom usage.

WP.174 The Need for Innovation to Halt AIDS among IV Drug Abusers (IVDA) and Their Sexual Partners

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New Jersey's AIDS population, now 5th largest in the U.S., is unique in that 62% of its cases are drug-related. Limiting the spread of AIDS in the marginal IVDA population has required abandonment of traditional public health approaches and creativity in developing a wide range of unproven prevention modalities. In other jurisdictions, authorities have distributed sterile needles, bleach for cleaning needles, and condoms to IVDA.

In New Jersey innovations have included hiring ex-addict street workers, distributing coupons for drug detoxification, and sending out mobile vans. IVDA are far less likely than gay persons to read about health risks; the street workers are able to warn them verbally of these risks. The coupons have been effective in drawing addicts into detoxification programs by gaining widespread attention and waiving initial fees. The mobile vans constitute a proactive step by going out to places where IVDA congregate to provide them with medical examinations, education, and AIDS counseling, rather than waiting for them to seek out attention.

Dealing with a difficult population such as IVDA requires continuing innovation. New Jersey is now focusing on education for the sex partners of IVDA, seeking them out in family planning and prenatal clinics.

WP.175 Underemphasis on Publicly-Funded Programs For Prevention of Transmission of HIV Among Gay Men and IV Drug Users.

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Government responses to the AIDS crisis have been called "too little, too late." However, with respect to preventing transmission (T) of HIV by blood transfusion, response was vigorous and prompt. We compared resources for prevention (P) of T by transfusion to those for P of T related to high-risk gay and bisexual/IV drug (G-B/IVD) activity in 1986 in an urban area of 900,000 population.

Cost of preventing transfusion-related T was $14,305/T prevented (9/80,000 units were anti-HIV +, 1.6 recipients/unit, $206,000 total cost of screening). In contrast only $87,920 was spent in programs for P of T among G-B/IVD, a population in which we estimate that: 1) at least 600 T occurred in 1986 and 2) a future public liability for health care costs over the next 5 years of $9,375/T, or $5.8 million total was incurred. We conclude that: 1) P of 9.3 cases of T (1.5% reduction) among G-B/IVD would justify the amount spent in P programs for this if programs for G-B/IVD were funded at the same rate as programs for transfusion-related T; 2) the public liability for future medical care for G-B/IVD-related T in 1986 was much larger (66X) than the amount spent for prevention that year.

The disparity between appropriate spending for prevention of transfusion related T and underfunding of programs to prevent sexual and IVD-related T must be addressed. The programs aimed at G-B/IVDU should prevent many cases of T and be very cost-effective in view of the high cost of treating AIDS in these groups, most of it public money.

WP.176 Non-Anonymous HIV Antibody Testing: Results in Colorado

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In July, 1985, the Colorado Department of Health (CDH) implemented a non-anonymous testing program for HIV antibody at 10 Testing Sites (HTS). Policies included collecting patient identifiers and risk behavior information on specially designed laboratory forms. The information is not revealed to laboratory staff but available to epidemiologists for analysis and followup. Confidentiality of records is protected.

Through December 1986, 10,476 tests (314.1/100,000 pop) were processed with 13.7% positive at Denver HTS (64.9% of tests), 9.6% at HTS outside Denver (19.1 % of tests) and 16.6% at non HTS providers (16.0% of tests). Most volunteered for testing due to perceived risk of infection. Only 1.7% claimed symptoms of HIV disease although 42.5% of this group were positive. Most (78.8%) tested were men with 16.1% positive compared to 2.2% positive in women. Differences in percent positive in men by sex preference were: heterosexual 4.1%, bisexual 16.1% and homosexual 27.3%.

Cited risk behaviors (RB) included: 18.4% denied any RB (3.4% positive), 48.4% claimed 1 RB (14.0% positive), and 33.2% claimed multiple RB (17.4% positive). Of those listing $\geq$ 1 RB, fewer (2.4%) of women were positive than men (18.2%). Of those with only 1 RB, sexual contact with homo/bisexual men was mot frequently cited by both men (78.8%), 19.6% positive) and women (43.6%, 0.3% positive). Negatives were less likely to return for results and prevention counseling than positives (77.5% vs. 88.3%). Patient identifiers allows follow-up of positives who did not return (129), as well as evaluation of the number of persons tested (9,267), and those who seroconvert (2.1%), linkage with AIDS reports, and efficient contact referral.

WP.177 Prevention of HIV Infection through Sexual Behavior Change.

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Given the critical role of education and behavior change in controlling AIDS we studied the efficacy of reductions in specific sexual behaviors as means of preventing HIV infection. Data used in the analysis come from a prospective cohort study of 360 NYC gay men in which HIV serologic data and detailed sexual histories were gathered. Linear logistic regression modelling was used to predict HIV antibody status as of 1986 from seven sexual activities (kissing and receptive/insertive anal intercourse, oral-genital sex, and oral-anal sex) measured for each of two prior annual time periods: Pre-AIDS, 1980-1981, and post-AIDS, 1984-1985.

Frequency of receptive anal intercourse during both pre-AIDS and post-AIDS periods were the only significant predictors of 1986 antibody status. The relationships held for all levels of number of partners. The efficacy of behavior change in preventing HIV infection was quantified by dividing respondents who engaged in receptive anal intercourse during the pre-AIDS period into: (i) those who stopped anal intercourse in the post-AIDS period, 1984-1985, and (ii) those who did not not stop in the post-AIDS period. Of those who stopped receptive intercourse, 22% were HIV positive as of 1986 while 45% of those who did not stop were positive (odds ratio=3.26, 95% CI 1.70,6.22). This effect is stronger for the most sexually active half of the sample. Among those with 15 or more partners in the pre-AIDS year, 26% who stopped receptive intercourse were HIV positive as of 1986,while 64% of those who did not stop were positive (odds ratio=5.02, 95% CI 2.13,11.74). These results indicate that behavior change, specifically eliminating receptive anal intercourse, can significantly reduce the likelihood of initial HIV infection among gay men.

WP.178 "RAP'N Down STDs, Drugs, and AIDS", A Community-based Approach to AIDS Education Among Minority Adolescents

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To stimulate AIDS awareness and education for minority adolescents, we piloted a cooperative community project utilizing RAP music to attract minority teens to participate in a "RAP'N Down STDs, Drugs, and AIDS" contest. The goals of the project were to create a fun, non-traditional approach for minority adolescents to become involved in their own learning about risk behaviors for AIDS and other STDs, and to stimulate community involvement and support with a highly-visible awareness campaign.

The Department of Public Health contracted with a major community organization to coordinate the project with 5 youth-serving agencies (YSA). Each YSA conducted promotion and educational outreach for a neighborhood preliminary "RAP Off", planned to coincide with the 1987 Valentine's Day and National Condom week. The finalists from the 5 "RAP Offs" competed for the grand prize of $500 on a popular television program. To win, contestants had to compose and perform a 60-second RAP about AIDS prevention. The RAPs of the finalists were recorded and aired as public service announcements on popular radio stations. This project may serve as a model for innovative community-based AIDS awareness and education campaigns for special populations in other metropolitan areas.

WP.179 A Multi-Media Campaign to Encourage Condom Utilization

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A multi-media campaign targetting young people aged 15 to 24 years was launched in April 1987 in the province of Quebec, CANADA. The primary message of the campaign focussed on encouraging condom utilization to prevent sexually transmitted diseases. On a limited budget, television, radio and print advertising was developed to coordinate with a public relations communications plan aimed at province wide penetration. Varied support activities, including the distribution of pamphlets, flyers and posters, were conducted by local health units to coincide with the campaign. Initially, difficulties were encountered in convincing networks to carry television advertising mentionning condoms even when presented in generic form by a health organisation. Considerable public debate was engendered during both the design and the implementation phases.

Pre- and post-campaign public opinion polls were conducted as one measure of the effectiveness of the intensive phase of the campaign.

WP.180 DRUG USERS' ORGANIZATIONS AND AIDS PREVENTION: DIFFERENCES IN STRUCTURE AND STRATEGY

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Organizations of homosexual men have provided services to persons with AIDS and ARC, educated gays about risk reduction, and given gay men a voice in AIDS policy and research debates. Intravenous (IV) drug users had less formal organization prior to the epidemic, and have been much slower to mobilize in response to AIDS. We have conducted field research on the Dutch *junkiebonden* (drug users' unions) and ADAPT in New York City. These drug users' organizations have distributed AIDS information to IV drug users both in person and through the mass media. *Junkiebonden* existed before AIDS was recognized; they have reacted to the epidemic in different ways. They have had internal conflicts over their goals and values, and external disagreements with public health and drug treatment agencies. They had previously initiated a system for exchanging used syringes for sterile ones, and have since taken part in the official needle exchange program, although at times organizational instability has detracted from their ability to dispense syringes. ADAPT, an organization of ex-IV-drug users, current IV drug users, and health professionals, was organized specifically to deal with AIDS. It has provided training to drug treatment agency staffs, and services to individuals with AIDS or severe ARC. ADAPT and some *junkiebonden* have taught individual drug users ways to reduce the risk of exposure to HIV or of transmitting it to others. On the basis of our observations, it appears that organizations in which ex-users and health professionals are dominant can provide consistent interventions which can motivate risk reduction among those drug users who are most open to change. It also appears that organizations of hard drug users are unstable, but when they are functioning well are more able to reach those street drug users who particularly distrust established institutions and to develop new values among drug users that will legitimate "safe injection" procedures among persons who continue to inject drugs.

WP.181 In Vitro Tests Demonstrate Condoms Containing Nonoxynol-9 Provide Effective Physical and Chemical Barriers against Human Immunodeficiency Virus

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In an in-vitro model 20 condoms (Ansell Inc., Dothan AL), 10 with 0.9 ml 6.6% (v/v) nonoxynol-9 (NX) and 10 without NX, were tested as barriers against human immunodeficiency virus (HIV). Each condom was mounted on a 20 cm hollow dildo and placed in a 15 x 5 cm glass cylinder containing 10 ml of HIV-free RPMI 1640 medium. 4 ml of cell-free and cell-bound HIV medium was placed inside the condom tip. To simulate intercourse, the dildo was pumped up and down 100 times. Samples were taken from the media inside and outside the condom for HIV cultures. Next the condom was ruptured. Again intercourse was simulated and samples cultured. All experiments were repeated in the reverse fashion, i.e. with HIV medium in the cylinder and HIV-free medium inside the condom tip.

	CONDOMS WITHOUT NX		CONDOMS WITH NX	
HIV medium	inside	inside	inside	outside
Sample from	outside pre-rupture	outside post-rupture	inside pre-rupture	outside post-rupture
Culture positive	0/10	7/10	0/10	0/10

Cultures were tested for HIV RT activity for 6 weeks. No condom without NX leaked HIV before rupture, but after rupture HIV could be detected in outside medium. In contrast none of the samples taken either before or after rupture of the NX containing condoms was positive. We conclude that undamaged condoms provide an effective physical barrier against HIV and that 6.6 % nonoxynol-9 diluted < 22 times after condom rupture may provide an effective chemical barrier.

WP.182 Community-Based Demonstration Project for AIDS Prevention and Risk Reduction: Organization of a Comprehensive Prevention Program in Denver.

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In 1986, DCS organized a comprehensive regional AIDS prevention program as part of a CDC-sponsored Community-Based Demonstration Project (DP) for AIDS prevention and risk reduction. The main purpose of the DP is to determine the most effective means for prevention of HIV transmission in populations at risk, predominantly through educational programs. Educational modalities include literature, posters, audio-visual aides, lectures and seminars, public service announcements, introduction of AIDS education into public school curricula, and skills provision training in populations at risk. An AIDS/HIV Information Service provides educational materials and newsletters, serves as a clearinghouse for new information, arranges seminars, has a phone response center, and networks with other educational groups.

HIV antibody testing and counseling and serial cross-sectional seroprevalence surveys are performed at an HIV testing and counseling site, STD clinic, IV drug use treatment centers, selected obstetric clinics, and blood banks. Populations studied include gay men, IV drug users, female prostitutes, high-risk obstetric patients, heterosexuals in a STD clinic, and military recruits. In addition, a large cohort of gay men is recruited for a prospective longitudinal study to evaluate different and innovative educational modalities and to elicit extensive information about knowledge, attitudes, and beliefs concerning AIDS and risk behaviors.

Measurements include serial seroprevalence studies; AIDS surveillance; rates of gonorrhea, syphilis and hepatitis; and questionnaire surveys in different populations. Within the cohort, behavioral differences between seropositive and seronegative, and seroconvertor and seronegative subjects will be analyzed. Organization of a comprehensive AIDS prevention program requires significant resources, long term planning, well-trained personnel, adequate laboratory and office facilities, cooperation with diverse communities and medical care providers, development of multiple education modalities, flexibility in response to changing needs, and ongoing evaluation.

WP.183 The 800 Men Study: A Controlled Study Of An AIDS Prevention Program In New York City

MICHAEL QUADLAND, W.D. SHATTLS, R. SCHUMAN, R. JACOBS

Since 1982, traditional AIDS education programs in New York City have imparted information about the disease and its transmission. To date there has been no systematic study of the effects of such programs on sexual attitudes or behavior. In October of 1985, 619 gay and bisexual men participated in a controlled study of pre- and post- test experimental design to evaluate the effects on sexual attitudes and behavior of four different education programs. It was hypothesized that a program which attempted to eroticize safer sex would be more effective than the traditional program, that the use of explicit erotic audiovisuals would be more effective than not, and that all three interventions in which participants met in groups would be more effective than an information-only, at-home control group.

It was found that: (1) there was a substantial amount of heterosexual activity in the sample; (2) most participants had already made substantial changes in sexual behavior, but approximately 40% were still at risk; (3) change in attitudes and behavior was associated with participation in a group educational experience; (4) changes in sexual behavior were observed in both the traditional and eroticizing programs; and, (5) the use of explicit erotic audiovisuals is more effective than not in promoting safer sexual alternatives. These findings are important in providing a rationale for a more positive approach to AIDS prevention which includes attempts to eroticize safer sexual behavior.

WP.184 Consequences of AIDS Antibody Testing Among Gay Men: The AIDS Behavioral Research Project. THOMAS J. COATES, S.F. MORIN, L. MCKUSICK, University of California, San Francisco, School of Medicine.

We followed 560 gay and bisexual men from November 1984 (before HIV antibody testing was available) until November 1985 and November 1986 (after HIV antibody testing was available) to determine the consequences of such testing on high risk sexual and drug use behavior, psychological distress, and relationship status. In November 1984 there were no differences between groups ultimately testing positive and negative in percent of men reporting high risk sexual behavior. After antibody results were found out, significantly greater percentages of those who found out that they were antibody positive ceased practicing unprotected active and passive anal intercourse. Also, the antibody positive group reported significantly greater stress and depression and their relationships were more likely to break up. The results of this study indicate that antibody testing may have positive public health outcomes. However, even though positive antibody status was associated with reductions in high risk behavior in those tested, it was also associated with potentially adverse mental health consequences. We found significant increases in stress and depression in the antibody positive group. Men in the antibody positive group were also more likely to have their primary relationships break up and to be celibate. More intensive study of antibody positive persons is needed to determine the full significance of these findings particularly for long-term mental health services.

WP.185 Targeted Outreach Techniques for Minority AIDS Education. RACINE WINBORNE, B. M. Branson, J. Stein, D. Vaughan, Health Education Resource Organization, Baltimore, MD, USA.

Disproportionate numbers of reported AIDS cases among Black Maryland residents prompted the development of targeted, culturally sensitive education efforts to improve AIDS awareness and prevention measures.

Questionnaires indicated that certain radio stations were more likely to reach the desired population, and that print media was much less effective. A bus poster was designed to advertise an information hotline phone number; the large number of callers who identified this poster as their source of information proved this to be the single most effective technique to deliver an educational message to a large segment of the Black population in Baltimore city. Community leaders were recruited for a Minority Task Force, and Black church organizations were solicited to provide educational forums; church leaders appeared in public service announcements.

Denial of the excess incidence proved to be the most significant barrier to initiating community-based educational programs. A series of educational presentations for tenants associations in the Baltimore City Housing Authority served to stimulate interest, and increase receptiveness.

WP.186 AIDS Antibody Testing: Who Takes the Test? STEPHEN MORIN, T.J. COATES, W. WOODS, L. MCKUSICK, University of California, San Francisco, School of Medicine.

This study presents data on reasons given by gay men for wanting to be tested for antibodies to HIV. Data were gathered in 695 gay and bisexual men in San Francisco who responded in May 1985 and 676 men who responded in November 1985, and 1986, as part of a larger ongoing longitudinal study. By November 1985 less than 31% had been tested even though anonymous and confidential testing had been widely available since July, 1985. The primary motivations for being tested were to reduce anxiety and uncertainty and to know if one was capable of infecting others. The primary motivations for not being tested were fears of increasing anxiety, perceptions that the test lacked meaning, and concerns about confidentiality and the potential for discrimination. Gay men in the sample were relatively well informed about AIDS and the meaning of the HIV antibody test. The respondents generally recognized that a positive test result did not necessarily mean that an individual would go on to develop a deadly form of AIDS. Most recognized that a negative antibody result could mean that the body had not yet produced antibodies to the virus and that it was possible to have the virus without antibodies. Our data suggested that the primary reasons for wanting or not wanting to be tested were psychological rather than medical Those who did not want to be tested believed that knowing that one had been infected would greatly increase one's anxiety and fear. Going through testing provokes anxiety as does living a life knowing that one has been infected with the AIDS virus. Community education efforts have resolved concerns about the meaning of the test and poor test validity. Those who did not want to be tested wanted to clear up ambiguity about past infection and to have good information so that they would avoid infecting others.

WP.187 An AIDS Education Outreach Program for Minority Communities JO ANN VALENTINE, Y. RIVERA, A. FREEMAN, C. HALEY, Dallas County Health Department, Dallas, TX

AIDS education in minority communities must emphasize messages to reduce fear and to increase the understanding of risk behaviors and focus on behaviors to reach persons who would not identify themselves to be in a risk group but who do engage in risky behaviors. In addition, AIDS education provided through traditional media channels has not adequately reached minorities without a program that actively identifies minority communication lines and persons of influence to deliver the messages.

The Dallas County Health Department has developed an active program of AIDS education outreach to the black and hispanic communities. The goals of the program are to identify community leaders on health issues, enlist their support in planning an approach and provide the information in a setting that allows attendance without being perceived as "needing" the information.

Social service organizations, community councils, minority professional groups, ministers, health care providers and radio personalities have been very effective in planning educational messages and in lending their support and increasing the credibility of the messages.

Minority populations have been reached in Dallas by addressing AIDS as a risk to sexual partners of IV drug users, persons with multiple partners and adolescents. Educational outreach has been most successful in churches, schools (after approval by parents), public housing tenants' association meetings and English as a second language classes.

WP.188 "AIDS as an Industrial Issue: The Australian Experience" MARK ANNS and ANDREW MORLET, Albion Street (AIDS) Centre, Sydney Hospital, N.S.W., Australia.

The industrial issues surrounding the AIDS epidemic have yet to be fully recognised in Australia. During the past two years several of Australia's major employers have had to provide services to employees infected by HIV, and to deal with widespread ignorance and fear. The Sydney AIDS Clinic has been used as an outside consultant by several of Australia's major employers, to advise on health and policy issues relating to HIV infection. This paper, using case examples, examines the types of problems employers have experienced: denial of a problem; absence of policies on infectious diseases; hysterical staff reactions to fellow workers with HIV infection and industrial, health and welfare issues relating to the identification of infected employees. It is argued, using case examples, that industrial problems can be minimised by a) recognising AIDS as having industrial remifications - both for occupational health and safety and staff welfare; b) the development of policies related to infectious disease; c) the provision of counselling/information and in-service training; and d) the use of outside consultants.

WP.189 Sexual Relations in Bathhouses in Los Angeles County: Implications for AIDS Prevention Education

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807 men at 7 bathhouses in Los Angeles County completed exit interviews in July and August of 1986. 61 percent participated in activities associated with low risk of HIV transmission, while 10% participated in passive and/or active anal intercourse without a condom, behavior associated with the highest risk of HIV transmission. In comparison, more of the high risk group were under 30 (46% vs. 34%), belonged to minority groups (41% vs. 27%), earned less than $20,000 annually (44% vs. 26%), had not attended college (24% vs. 12%), had 5 or more male sexual partners in the past month (46% vs. 25%), and participated in fellatio without a condom (60% vs. 20%) (all $p<.05$). Similar proportions reported familiarity with information in the bathhouse on AIDS (96% vs. 98%) and felt it played a role in their understanding of AIDS prevention (84% vs. 86%).

These data indicate that the majority of highly sexually active men who attend bathhouses in Los Angeles County now practice low risk sexual behaviors. However, improved programs directed toward those young, minority, low income, less educated men who are at highest risk of HIV transmission must be developed as soon as possible.

WP.190 Blood Donation Histories of Reported AIDS Patients.
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Patients meeting the national case definition for AIDS are reported to CDC on standardized case-report forms that include a question on blood/plasma donations since 1978. Between March 1985, when test kits to detect antibody to HIV were licensed for screening blood, and October 31, 1986, 17,387 AIDS cases were reported to CDC. Among the 9,143 (53%) patients who answered the blood donation question, 394 (4%) gave histories of blood donation since 1978, but only 25 had donated since March 1985. Of the 25 recent donors, 23 were men; of these, 13 were bisexual, 9 were homosexual, and 1 was a heterosexual IV drug abuser. The 2 women were heterosexual partners of high-risk individuals (a bisexual male and an IV-drug abuser). Eighteen (72%) of the recent donors were white; 5 (20%), black; and 2 (8%), Hispanic. When compared with all reported AIDS patients, those answering "yes" to the blood donation question were more likely to be white and bisexual. Since intensive screening of blood donors began in the spring of 1985, some members of high-risk groups continue to donate blood or blood products. Although still important for preventing transfusion-associated AIDS, blood donations by high-risk individuals suggests an even larger problem in the broader effort to prevent the spread of AIDS: persons who do not perceive themselves at high risk and therefore ineligible for donating blood may also not perceive the need to engage in risk-reduction behaviors. Since our data pertain only to reported AIDS cases and do not include the larger pool of HIV-infected persons without overt AIDS, the risk awareness problem may be considerably greater.

WP.191 A Modified System of Contract Tracing for HIV Seropositives
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Control strategies for sexually transmitted diseases (STD's) must be appropriate, effective and acceptable. Both formal contact tracing, where a public health worker notifies named sexual partners, and simplified contact tracing, where the index patient does the notification, are well accepted methods of STD control. A simplified system is usually used for AIDS patients and HIV seropositives. A formal system of naming contacts to an interviewer would be unacceptable and counter-productive in HIV infections.

There may be contacts, however, whom the seropositive patient wishes to be notified but will not himself notify because of inability, fear or embarassment. Public health officials should make themselves available to locate such contacts. This is especially important since such contacts may include persons who have no suspicion of HIV exposure, for example, female sexual partners of unacknowledged bisexuals.

In British Columbia, HIV seropositives are requested to anonymously submit to STD control authorities identifying information on contacts they themselves will not notify. These sexual partners exposed to HIV are then located through the traditional public health infra-structure, notified of the exposure and offered information, counselling, antibody testing and support. This system has found acceptance and support from all groups involved in AIDS and early results are encouraging.

WP.192 The National Condom Awareness Project: A National Survey of Knowledge of AIDS, Use of Condoms and Sexual Behavior Among College Adolescents
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The National Condom Awareness Project (NCAP), presently underway, is a survey assessing college-age adolescents' knowledge, attitudes and misconceptions about AIDS, use of condoms and type and frequency of sexual practices.

Approximately 2,000 college undergraduates matriculating at 18 major universities geographically-distributed in the United States are participating in the project. Students complete an anonymous self-report questionnaire designed to elicit information about knowledge of AIDS: transmission, prevention and misconceptions, knowledge of other sexually transmitted diseases, attitudes regarding perceived risk of HIV infection, use of condoms, decision-making processes which influence the risk of engaging in high-risk sexual behaviors and type and frequency of sexual practices. Data will be presented describing geographic, ethnic/racial and gender differences as well as the interrelationships between knowledge of AIDS, perceived risk of HIV infection, type of sexual practices and use of condoms. The NCAP can be useful in providing baseline information on this population as well as in the planning, development and implementation of public health and college-based AIDS risk-reduction education programs for adolescents.

WP.193 AIDS Education Options by the U.S. Health Insurance Industry
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Without any known curative therapy or vaccination for HIV infections, prevention through education will remain a cornerstone for stemming the epidemic. Every potential avenue of education needs to be explored in attempt to reach all populations. We hypothesized that the US Health Insurance Industry (HII) may have altruistic and fiscal incentives to provide AIDS education for their subscribers. A confidential telephone survey of 24 HII companies with offices in the S.F. Bay Area was undertaken (1) to determine what kind, if any, AIDS education had been provided for subscribers, and (2) whether or not these HII companies would be interested in providing AIDS education. This survey was completed prior to the Surgeon General's or Nat'l. Inst. of Medicine's Reports about AIDS. Appropriate administrative officials of each company were interviewed by phone.

All respondents indicated that education on transmission is an important means of prevention. 54% of HII companies had received or attempted to receive educational materials on AIDS. None had actually provided information on AIDS to subscribers. 72% felt their subscribers could use more information about HIV transmission. 60% felt it was in their company's best interest to provide information on AIDS transmission to their subscribers and that providing such information would lower the incidence of HIV infections in their subscribers. These data indicate that a semple of the US HII has not provided AIDS information for their subscribers, but would do so to decrease the incidence of HIV infections. AIDS education by the HII represents a viable means of HIV educetion and implementing such a policy will decrease the spread of HIV in the US and elsewhere.

WP.194 Changing the Public Debate on AIDS: A Need for a Communal or Societal Approach to The Problem.
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In the absence of effective medical therapy, control of the AIDS epidemic requires the dissemination and acceptance of complex and controversial educational messages. The nature of the public debate has undermined our ability to delivery effective education to the public. Examples include (1) discussions of anal-genital intercourse as dangerous (as opposed to any intercourse with an infected person being dangerous), (2) comments about AIDS not being a threat to the "general population" (as if the 1.5 million infected persons are not the "general population"). Statements such as these stimulate the public's perception that AIDS is "their" (gay and drug users) problem, not "our" problem and heighten the public's sense that "they", the infected, may give the disease to "us", the healthy. It is only by emphasizing the communal nature of the AIDS threat and seeking from all members of society an increased measure of trust and sacrifice can the public debate on AIDS result in positive steps directed towards decreasing transmission.

In the absence of a communal or societal view of the epidemic, the public debate will become increasingly rancorous as uninfected populations begin to feel more threatened. The result will be increasingly oppressive social legislation (mandatory reporting or testing, quarantine, etc.) put in place as "quick fix" solutions that are usually counterproductive to the aim of slowing transmission. Examples of such processes are already visible-six states have mandatory reporting of HIV seropositivity (an obvious disincentive for testing). A societally centered public debate is essential to avoid an acrimonious and adversarial public fight over how best to control the AIDS epidemic.

WP.195 Lessons of History: What Really Works in Reducing STD Rates?
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With the realization that the HIV epidemic heralds a catastrophe for American society, scientific and social organizations have called for massive educational efforts costing hundreds of millions of dollars. What can we learn from past experience about the effectiveness of such programs?

Because the introduction of sulfonamides and penicillin in the early 1940s so effectively treated gonorrhea and syphilis as to eliminate Venereal Disease treatment as a medical specialty, the experience of controlling sexually transmitted diseases by social engineering has been lost.

A massive unitary US Army program to educate and protect soldiers from sexually transmitted diseases was implemented in 1911.

The effects of this massive program may be seen in the statistics for STD in American troops stationed in the Panama Canal Zone from 1911 to 1922.

1911-118	1913-197	1915-137	1917-124	1919- 83	1921-154
1912- 69	1914-136	1916-116	1918- 67	1920-139	1922-144

The drop in 1912 reflects confusion over the beginning of the program. The sharp drop in 1918 and 1919 reflects the takeover of the cities of the Zone by military authorities as decreed by Treaty during the time of declared war in Europe with the authorities immediately and vigorously suppressing prostitution. The standardized education, inspection, distraction, and punishment campaign had no perceptible effect whereas the suppression of prostitution had a clear and dramatic effect, but even then the rate was halved, not brought to zero.

WP.196 Inter- and Intra- Personal Factors in the Recruitment and Retention of Research Subjects For an AIDS Intervention Research Study
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University AIDS researchers and staff and volunteers of a community AIDS service organization have collaborated to design and implement a multi-year study on the effects of stress, psychosocial variables and exercise on the health and immunologic status of gay men at risk for AIDS. More importantly, the study will evaluate the efficacy of exercise and stress reduction techniques as buffers of possible adverse effects of stress on health and immune function. Observation and subject reporting of the initial three groups of subjects (N=25), have revealed several inter/intrapersonal factors that have implications for the success of this type of research project with this population. Some of these factors are: that subjects move through several psychological phases including engagement, affiliation, committment and termination; that voluntary participation in the study requires that high risk men accept the realities of their risk factors, confront the anxiety related to disclosure of HIV status and immune function, develop group identity with other subjects, commit to attendance at frequent study-related appointments, and integrate new patterns of stress reduction and exercise into their lives; that substantial staff support has been necessary to adequately obtain informed consent, provide crisis counseling after disclosure of HIV positivity, encourage discussion of feelings related to behavior change, and; that subjects themselves serve to perpetuate the study by becoming spokespersons, exercise trainers and recruiters. (Supported by grant No. 1 P50MH42455-01 from NIMH).

WP.197 "AIDS Community Outreach for Intravanous Drug Users" Harvey W. Feldman, Ph.D. & Patrick Biernacki, Ph.D. YES Project, 1779 Haight St., San Francisco, CA 94117.

In May 1986, a community health education/outreach program was created in San Francisco to stop the spread of AIDS among intravenous drug users (IVDUs). Currently, the program employs eight workers who provide AIDS education, counseling and referral to drug users in those areas of the city that contain the highest concentrations of IVDUs. This paper describes and analyzes the major stages undergone since the program's inception and addresses problems encountered. The analysis will help other communities to develop similar outreach efforts.

The program developed in the following stages: 1) Formation of the overall strategy guiding the program effort toward the major goal of stopping the spread of AIDS among IVDUs; 2) Ethnographic studies of target areas to map out & analyze the needle-using scenes and drug-using practices; 3) Recruitment & training of an outreach staff component; 4) Successful entree into the target community; 5) Development & distribution of health promotion materials, condoms and small bottles of bleach; 6) Use of indigenous field assistants, who are natural leaders, to help promote safe health practices; 7) Utilization and management of the media to promote the project's goals; 8) Evaluation and reassessment of project plan and ensuring compliance with health messages, & 9) Entry into new IVDU scenes, when and how to move beyond the original target groups.

An administrative project evaluation indicates that, contrary to popular wisdom, IVDUs will change their behavior, especially in relation to sanitizing their shooting paraphernalia.

WP.198 Patients with Kaposi's sarcoma who opt for alternative therapy: immune and psychological measures.
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Twenty four men who have chosen a holistic approach to their diagnosis of Kaposi's sarcoma have been studied sequentially. They are all following a macrobiotic regimen. The median survival for the 8 men who have died is 19 months (range 5-46 months). None of the surviving members of the cohort have required hospitalization. One has required local radiation. Four are alive 3 or more years after diagnosis. Contrary to what might be expected, the number of lymphocytes in the group has increased with time over the first 3 years after diagnosis (r=0.474,p=0.006). The number of T4 cells increased over the first 2 years after diagnosis (r=0.458,p 0.03). The percentage of T8 cells was unchanged (r=-0.06,p=0.69). A subset of approximately 1/3 of these patients have filled out psychological questionnaires,including the Beck Depression Inventory (BDI) and the McNair's Profile of Moods Survey (POMS). Preliminary data suggests these men are generally less depressed (median BDI score 10, range 1-28),less anxious (median POMS Tension score 4,range 3-6),and feel more energetic (median POMS Vigor score 23,range 8-32) than has been reported for other cohorts of men with AIDS. The psychological profile associated with this group is hypothesized to have a beneficial effect on the clinical course of their disease.

WP.199 Patterns of Distress Following HIV Antibody Test Notification.
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The psychological impact of informing at-risk individuals of their HIV antibody test results is assessed in a group of 108 gay men from San Francisco, 66 of whom elected to be notified of their results. Of those notified, 44 were seropositive and 24 were seronegative. We compare self-report measures of psychological distress and potential psychosocial mediators prior to receipt of results, and again two weeks and three months following their notification session.

We found a small, but significant, ($p<0.03$) increase on the Beck Hopelessness Scale, but no significant increase in several other measures of distress following notification of seropositives. We found a significantly higher perceived risk of developing AIDS at baseline ($p<0.01$), among both seropositives electing to know their results than among subjects who elected not to know. This difference persisted at three months post-notification even among those notified of a negative serostatus.

This lack of substantially increased distress following notification of seropositives may be explained by the subjects participation in a prospective epidemiological study which has returned clinical and immunological information to participants, and by participants' expectation of their serostatus (96% of seropositives correctly anticipated their serostatus). Our group may resemble many at-risk populations in having long considered themselves to be seropositive, and so at decreased risk of severe adverse psychological reactions to antibody test results.

WP.200 The Unique Counselling Interventions Required for Intravenous Drug Abusers (IVDAs) with AIDS/ARC and their Families
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The psychosocial and economic realities surrounding people infected with HIV who are IVDAs, or sexual partners of IVDAs warrant particular counselling interventions. The population is predominantly poor, black, and hispanic for whom the diagnosis of AIDS compounds pre-existing social and economic stressors, as well as the effects of long term chronic drug abuse.

Systems must be set up to provide an interdisciplinary approach in a coordinated and integrated manner from diagnosis to death. Entire families become the clients - be they parents and babies who are all sick with AIDS/ARC or infected with HIV or be they adult siblings who used IV drugs together and are now being cared for by other family members.

Counselling interventions are directed at the emotional and social impact of an AIDS/ARC diagnosis in conjunction with the unique pre-existing psychosocial variables in this population. Some of these include: 1)that day-to-day survival issues are frequently the primary psychosocial concern, 2)the sense of alienation and expendability already experienced that is compounded by the diagnosis, 3)the feelings of low self esteem absorbed from society's view of the associated high risk behaviors this diagnosis may reinforce, 4)that drug abusers may have severed relations with family and become particularly isolated.

For health care providers to provide compassionate care, as well as in order to disseminate proper information regarding transmission of HIV to IVDAs and their sexual partners, systems must be established that address the particular needs of this population.

WP.201 **A Longitudinal Study of Distress and Coping In Men with AIDS and AIDS Related Complex**
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The problems associated with AIDS spectrum disorders transcend the medical dimension of the disease. In a 5-year study, we are documenting the psychosocial impact of events that occur along the disease continuum. Fifty gay or bisexual men with AIDS, recruited from San Francisco General Hospital, were administered a battery of standard self-report measures of distress and coping 2-8 weeks after diagnosis, and then 4, 7, and 15 months later. Fifty-three men wit ARC were administered the same battery at the same intervals except the 4-month follow-up.

Surprisingly, the number of self-reported AIDS-related "hard" or "soft" symptoms were only correlated with two measures of distress at the initial assessment for men with AIDS, and were not associated with distress at any follow-up point. At the initial assessment point, men with ARC reported--unexpectedly--higher levels of anxiety, confusion, depression-dejection, fatigue-inertia, tension, and anger-hostility than men with AIDS. Seven months later, however, these group differerences had diminished. Men with AIDS were significantly more confused at the initial assessment than at 4-month follow-up, and were significantly less anxious 7 months later. Men with ARC were significantly more anxious 7 months later than initially, but also significantly less hopeless. The psychological coping style of "Hardiness" was significantly negatively correlated with all scales of distress and mood at initial assessent for men with ARC. In a multiple regresison analysis, less Hardiness was the best predictor of overall distess. Hardiness played less of a role, however, in affecting distress for men with AIDS, or for men with ARC at follow-up assessments. Data for the 15-month follow-up will be presented, as well as implications for psychosocial interventions.

WP.202 The Importance of Supportive Interventions for Caregiving Family/Friends during the AIDS Crisis.

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Long term institutional care for AIDS or ARC patients is often unavailable in many communities. After periods of hospitalization the burden of continuing care may fall upon the patient's family and/or friends. These caregivers have become an important resource in the overburdened AIDS treatment network. Consequently it is vital that they be given the support and training necessary to enable them to persevere despite overwhelming obstacles.

As Co-therapists of ongoing grief recovery groups over the past three years, we have observed surviving family members and friends as they related difficulties encountered relative to their unmet needs during the period preceding the patients's death. Many in this already high-risk population found themselves without adequate social, legal, financial or emotional supports; knowledge of available community assistance programs; or nursing skills to care for the patient at home. They were neither able to communicate with health care professionals nor understand and cope with changes in their relationships. They tended to experience more depression, fatigue, guilt, anger, helplessness and illness both before and during the mourning period than did survivors who felt that their needs were met.

We offer a program of education and supportive interventions that could free these caregivers to continue a level of essential care by reducing immobilizing stresses. This ancillary support network for health professionals and persons with AIDS/ARC will then be maintained.

WP.203 Providing Psychological Support to Children with AIDS

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There have been approximately 400 children with AIDS reported to U.S. Centers for Disease Control, and estimates of over 3,000 unreported or undiagnosed cases. A large percentage of these children, 80% of whom are the offspring of IV drug abusers, are in the New York metropolitan area. Limited social and educational services, as well as a lack of advocacy for children with AIDS is common. In December of 1985, the Gay Men's Health Crisis began a volunteer program serving children with AIDS and their families. All direct services are provided by volunteers, in hospital or at home. The "Buddies" provide social and developmental stimulation for children, while "Crisis Intervention Workers" are focused on emotional support for parents and caregivers, child advocacy,referrals to social services and entitlement programs. So far, we have worked with 25 children, between 12 months and seven years of age. Problems of these children and families, as well as services provided will be reported.

WP.204 Fostering and adoption of infants at risk of HIV infection

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To date we have cared for 25 babies at risk of acquiring HIV from 24 mothers. Three mothers acquired the HIV infection by heterosexual contact the rest via intravenous drug misuse although only 9/21 are currently abusing. Eight out of 24 were single parent families and there were immediate demands for adoption or foster care.

Thirty four foster families offering places to babies were approached and following interviews 3 offered to care immediately for a high risk baby. Twenty seminars followed, initially conducted by a social worker and physician and latterly by a social worker resulted in 12 further families being identified for these infants. To augment all family placements, a pool of 20 specially prepared nursery nurses are available to cover family illness. Short term emergency care was provided by an Infectious Disease Unit but to date no at risk, or high risk child has required long term hospital or residential care in Edinburgh.

The likelihood of children returning home diminishes with the length of time in care and plans are being made for the future of the fostered children. The local authority's commitment to giving children as normal a life as possible in securing foster and adoptive families has been aided by well prepared, flexible families who care for children with a range of special needs. The general method is now being adopted by other local authorities faced with similar potential problems.

WP.205 Nurse Recruitment and Screening of Patients for AIDS Research Protocols

MARGARET MEGILL, B. HERPIN, B. BAIRD, National Institutes of Health, Bethesda, MD. As the number of AIDS cases and the number of investigational drug studies have increased, an efficient yet individualized screening process for matching patients to particular protocols is required. In order to focus and expedite patient recruitment efforts, protocol-specific checklists were formatted by the nurses and used in their telephone communication concerning 760 referrals. Among the elements found to be most valuable were relevant patient history (Kaposi's sarcoma, type of opportunistic infections, current symptoms), hemoglobin, and T4 numbers. A cut-off of 200-400 T4 cells was found to be helpful in distinguishing patients with a high risk of developing an opportunistic infection during study. Following initial telephone selection, 277 patients were scheduled for a screening visit to NIH, limited to HIV culture of blood, an immune profile, CBC/diff, SMAC chest x-ray, and a brief nursing interview. Obtaining a chest x-ray at this early point in screening helped identify patients with unsuspected abnormalities who were not appropriate candidates for research but who required routine medical follow-up. Utilizing personal computers and the NIH DEC-10 system, a computerized data retrieval network was established into which results from either the clinical pathology laboratory or the various research laboratories were entered as generated. Once data collection was complete, the patient was reviewed by the research nurses and the senior investigator, a decision made as to protocol eligibility, and the patient and the referring physician notified. Only then were history and physical scheduled for suitable research candidates, of whom approximately 83 of 107 were found to be protocol eligible. Thus, preliminary phone and blood screening evaluation may greatly enhance the efficiency of screening patients for research protocols.

WP.206 Dilemmas of an AIDS Residence Program: the Legal, Ethical and Psychosocial Issues Integral to a Program and its Residents

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Now existing in many parts of the United States and Europe, housing programs for people with AIDS are a vital community resource. By coupling stable, low-cost housing with advocacy services, AIDS residence programs enable PWAs to remain as independent as possible, in a supportive home-environment.

Such programs do not always run smoothly. In spite of -- or perhaps because of -- proceeding "with the best of intentions," AIDS residence programs are forced to continually re-evaluate the ways they operate.

What flexibility is needed in interpretting program policies? How does a program carefully screen applicants without discriminating against the disease itself? What must a program know about tenant rights and probate? How sick is "too sick" to live independently? How does a program avoid inter-agency combat-zones?

This paper provides case studies demonstrating ways in which Shanti Residence Program has, since 1983, dealt with these and other issues. It hopes to increase sensitivity and problem-solving capabilities of persons who interact with -- or hope to form -- AIDS residence programs.

WP.207 View From Within - Coping With Isolated Thrombocytopenic Purpura

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The significance of how individuals perceive themselves and their illness and the effect on recovery has too often been given inadequate attention. This paper reports the results of the interview data and the drawings of eight homosexual males with Isolated Thrombocytompenic Purpura who participated in research on the impact of a psychophysiological intervention on psychological, physiological and immunological parameters. At the study's onset an interview was conducted in which questions of the meaning of the illness, its timing, previous approaches to coping with crisis, life changes which they desired to make, and factors considered important for maintaining their present level of functioning were asked. In subsequent interviews discussion focussed on coping, and changing perceptions of life and its meaning. Interview responses were compared with adults with acute leukemia undergoing induction chemotherapy. The latter although mentioning their own resources emphasized the help to be provided by doctors, nurses and chemotherapy. The men with Isolated Thrombocytopenic Purpura noted their own inner resources. This was substantiated by the cancer Locus of Control Scale. The homosexual males as compared with three other groups were higher on Internal scores and lower on those for Chance and particularly, Powerful Others. Changes in self perception over time were indicated in drawings in which participants depicted themselves, their illness, mood changes and approach to life.

WP.208 Evaluation of an Educational Program to Help Perinatal Nursing Staff Provide Care to HIV Infected Patients

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The increased incidence of perinatal HIV infection has had significant impact on nursing care practices in Labor and Delivery and the Nursery. Nursing staff education and support are necessary to circumvent exaggerated fears of AIDS. At SFGH an educational and support program has been developed to facilitate high-level nursing care standards as well as appropriate multidisciplinary patient management.

Program methods were: 1) a baseline survey of knowledge and attitudes about AIDS prior to the intervention program; 2) a multistage intervention program extending over a 4 month period, and 3) a post-intervention evaluation examining knowledge, attitude, and behavior changes. Intervention programs were for all nursing staff in Nursery and Labor and Delivery (N=45). Strategies included open staff meetings, didactic programs, onsite reinforcement, and implementation of perinatal HIV infection control guidelines.

Results: Changes observed included increased knowledge about HIV transmission and infection control. Staff also demonstrated increased sensitivity to more appropriate discharge teaching and made increased numbers of referrals for follow-up. Some nurses increased their skills in providing patient education about prevention of HIV transmission. Attitude changes were less predictable and more complex. Changes tended to proceed through several stages, but most staff reported reduced fear and more confidence in caring for HIV infected patients.

WP.209 Nursing Staff Knowledge, Attitudes and Self-Reported Behavior with Respect to Patients with AIDS.

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AIDS has evoked considerable fear and anxiety in the general public and among health care workers. A study of the attitudes, knowledge, and self-reported behavior with respect to AIDS of a group of 135 nurses and student nurses, 126 of whom worked in a large municipal hospital in NY City with an average daily census of 14 patients with AIDS or ARC, was done. A questionnaire was administered between 9/12/85 and 11/5/85. Confidentiality was ensured. Demographic data were obtained and subjects were asked to rate on a 5 point Likert scale 115 statements. All statements were ordered randomly and both positive and negative phrasing were used. Sixty-six statements dealt with knowledge, attitude and self-reported behavior in relation to AIDS and AIDS patients. For comparison, 16 of the statements were repeated with respect to three other diseases, which shared with AIDS the possibility of transmissibility (tuberculosis), of patient behavior in causality (emphysema), or both (hepatitis).

This initial survey found that while these nurses shared the fear and anxiety of the general public about AIDS, (57% worried about hospital transmission of HIV and 44% worried about the risk to themselves of opportunistic infection), they were able to make distinctions as to the risks to themselves and other patients, based on current knowledge about the four diseases surveyed, for 12 out of 16 disease comparison questions ($p<.05$). Although AIDS patients were blamed for their illness by 7-37% of the nurses, most nurses (72-87%) demonstrated a consistent attitude of compassion. Risk group was not a factor. This study instrument appears to be a valid means of assessing staff knowledge and attitudes towards patients with AIDS.

WP.210 Cost of Medical Care for AIDS in Massachusetts: Trends over a two year period

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Our previous work indicates that the inpatient cost of medical care for a group of 45 AIDS patients treated at one Boston hospital is $42,517 per patient per year. To evaluate the consistency of cost over time and by institution, a two year study of all 215 AIDS patients treated at 5 Massachusetts hospitals was conducted. These patients represent 75% of all AIDS patients treated in the state during 1984 and 1985.

Preliminary results indicate that the yearly inpatient cost per patient at each site varied from $42,517 to $63,477, and the cost was inversely related to the total number of AIDS patients treated at the site during the study period. Over the two year period, each study site showed a decrease in cost and the mean cost per case decreased from $50,087 to $36,996 ($p<.01$). The observed decrease was related both to shorter lengths of stay (mean 15.7 days/hosp. down from 19.2 days/hosp.) and a decrease in the mean number of hospitalizations (2.2/patient to 1.9/patient).

The results of this study indicate the inpatient cost of treating persons with AIDS is declining. Clarification of this data will become important as the epidemic spreads into areas of the country with few AIDS cases to date.

WP.211 Service Characteristics of U.S. Public and Teaching Hospitals with AIDS Patients

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A 1985 AIDS survey of 450 major U.S. public and teaching hospitals conducted by the National Association of Public Hospitals and the Council of Teaching Hospitals has yielded responses from 223/450 institutions. These hospitals, which treated almost 5,000 patients in the calendar year, were asked to identify the presence or absence of the following services to AIDS patients: separate AIDS unit; specifically designed system to monitor or track patients on an outpatient basis; a formal suicide watch program, training protocols for AIDS staff in hospitals ; education programs for non AIDS staff; formal linkages with various community groups representing high risk populations (homosexuals, minorities, drug users, hemophiliacs, women at risk).

Responses were analyzed according to four major institutional characteristics: hospital size, location, ownership and number of AIDS patients served. Findings describe similarities and differences among the institutions with regard to tendency for hospitals to establish AIDS units, the extent and type of hospitals able to coordinate and integrate inpatient and outpatient care, the emphasis on formal suicide prevention approaches, the extensiveness and sophistication of AIDS training programs, and the extent to which hospitals coordinate AIDS treatment with the key community groups.

WP.212 Comprehensive Case Management Utilizing Hospice Concepts: A Statewide Program

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New Mexico AIDS Services is the only AIDS service organization in New Mexico and offers case management services for all persons with AIDS/ARC in this rural state. Case management is based on the Hospice concepts of: a wholistic view of client needs, an interdisciplinary team approach to meet those needs and the promotion of quality of life. We utilize trained volunteers and existing community resources to reduce hospital in-patient days and therefore the cost of patient care by increasing in-home and out-patient support.

The case manager's role includes acting as: a client advocate; an educator-resource person to medical professionals; and a coordinator of support services. Another important element of a case management program is counseling of PWAs in regard to: living wills, power of attorney, medical guardianship, right to refuse treatment, informed consent and confidentiality.

The development and delivery of a comprehensive case management program involves establishing liaisons with existing services that provide in-patient acute and long term care; homecare and hospice nursing; delivery of meals and homemaker services; transportation, social service counseling for disability income and financial support. These liaisons optimize out-patient support and promote the education of community resource persons. To assure services to clients who live in rural areas the case manager must identify and educate health care professionals and appropriate resources in those areas by offering inservices, guidance and support.

The case management services are offered in adjunct with an emotional support and counseling program and are available on a 24 hour a day basis.

WP.213 Enhancing the Coping Skills of Families of Children with AIDS

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The AIDS program at Children's Hospital of NJ is a multidisciplinary, multiservice program that utilizes a chronic illness model in providing care to children andsupport services to their families. In 46/50 families with a child with perinatally acquired infection, diagnosis in the child resulted in identification of a primary caretaker (30/50) and sibling (7/50) with HIV infection. Initial response to the diagnosis included prolonged (longer than 3 months) denial in 12/50. In 6/12 denial interfered with acceptance of services for the child. Development of symptoms in the parent was associated with improved utilization of services for the child. Primary caretakers identified a need for asisstance in the following areas: access to entitlements (welfare, medicaid, WIC) 31/50, transportation 27/50, housing 16/50, school entry 9/50, decision making related to medical care 30/50, assistance with family problems unrelated to AIDS 30/50, medical care and service for the parent 12/50. When provided with the opportunity for ongoing therapy, 1/10 parents followed through on the referral. The social worker's role is to assist the caretakers to define their own needs realizing that the perceived need may be for concrete services rather than counseling and psychological support. Social work interventions are directed towards linking families with services and helping families adapt to chronic illness.

WP.214 A Hospice's Response to the AIDS Dilemma
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The Connecticut Hospice, Inc., the first hospice in America and the only teaching hospice to offer ACCME credits through its Institute training programs, examined in Dec., 1983 the question of whether the current criteria for admission to Hospice inpatient and home care settings allowed for the admission of patients with AIDS. On April 11, 1984 the Medical Board voted that such criteria did fit. Between April, 1984 and July, 1985 a series of steps were undertaken to implement this decision including: multiple inservices for paid and volunteer staff and families on infection control aspects and psychosocial issues involving the State, user-friendly hospitals, Shanti Project in San Francisco; the administration of Hepatitus B vaccine to all patient caregivers. The first person with a diagnosis of AIDS was accepted in July, 1985.

Since then Hospice, inpatient and home care, has seen many patients (12 case reviews) with a diagnosis of AIDS with various causes of onset and has worked extensively on psychosocial issues with those patients, families and significant others. As this Hospice is a statewide facility and these patients have come from all over the State, there has not been a time when it has not accepted a referral (AIDS). In recognition that there has been several patients who have been inappropriately institutionalized in acute care settings who are neither eligible for hospice inpatient and do not have a home, this led Hospice to undertake a hospice home for the homeless.

WP.215 Prospective HIV Serologic Survey of Employees in a Canadian Teaching Hospital
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1,496 employees at a 780 bed teaching hospital in Montreal have been enrolled in a prospective survey for evidence of HIV infection beginning June 1985. Work-related exposure to HIV and hepatitis B are being assessed by 6 monthly questionnaires and blood tests. During this study, 56 cases of AIDS have been diagnosed, resulting in 106 hospitalizations. The cohort includes 344 men, employed 3.5 years ± 3.8 (SD), and 893 women, employed 2.6 years ± 2.3, and 259 new employees (53 men and 206 women), working less than one month. The cohort consists of 275 administrative personnel without patient contact (18.4% of the entire cohort); 322 support and maintenance personnel with variable patient contact (21.5%); 93 physicians (6.2%); 614 nurses (41.0%); and 192 laboratory technicians (12.8%). Sera were assayed for HIV antibodies by ELISA assay; the nspecificity of repeatedly reactive sera was verified by Western blotting and an immunoblot assay, using cloned gp160.

Sera from 10 employees were repeatedly reactive on HIV-ELISA testing: 4 subjects were initially reactive (2 male and 2 female) and 6 were initially negative but found to be reactive 6 months later (4 female and 2 male). Only one male with a history of sexual exposure to HIV was seropositive by Western blotting and gp160 immunoblotting.

This study has failed to identify occupational risk for HIV infection, associated with hospital work, and confirms the very low prevalence of HIV seropositivity in urban non-risk populations in Canada.

WP.216 Evaluation of the antiviral activity and tolerance of HPA23 in 38 patients with HIV related disorders.
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22 AIDS (12 KS, 7 OI, 3 KS/OI) and 16 preAIDS patients staged according to the Walter Reed classification (3 WR5, 4 WR4, 1 WR3, 8 WR2) entered a HPA23 protocol: 2 IV injections per day (3mg/kg/day) during 14 days. 48 treatments were provided. 7 patients had a thrombopenia<150 000 before treatment. After treatment 15 patients had a reversible thrombopenia<100 000 (5<50 000).

Reverse transcriptase activity was studied by culture and coculture of the blood and CSF before treatment. Viremia was studied in 17 cases after HPA. Coculture was taken into account only when culture was negative. On blood cultures, viral inhibition was defined as a decrease of at least 400 000 cpm or a delay 10 days of the reverse transcriptase peak, failure as an increase of the activity and stability as no significant modification. Considering viral activity in the blood, among 6 patients with positive CSF culture before treatment, we noticed 2failures, 2 inhibitions, 2 stabilities. Among the others, we noticed 2 failures, 7 inhibitions and 2 stabilities. This study confirms that a short HPA23 treatment appears to inhibit viral replication in blood, and side effects are not limiting factors. We suggest to carry on this study with higher dosages and shorter courses which could be repeated every 2 months.

WP.217 Mycobacterium Avium Complex Isolated from the Lung Only, Does it Disseminate? TIMOTHY P. MESS. San Francisco General Hospital, San Francisco, U.S.A.

In December 1986 a retrospective review was conducted to investigate for dissemination of Mycobacterium avium complex (MAC) in AIDS patients who had culture proven MAC from the lung only. From January 1982 to October 1986, 107 patients had MAC cultured from the lung at SF General Hospital (SFGH). 22 of these patients had negative blood cultures for AFB at the time of their positive lung isolate. 16 of these 22 had follow-up AFB blood cultures of >1 month to investigate for dissemination and in 5/16 (31.3%), these cultures were positive for MAC. The last negative blood culture was at 21-224 days (median 100 days). The first positive blood culture was at 24-280 days (median 171 days). All 5 patients had significant diarrhea preceeding their MAC blood isolate. 2 had cryptosporidium, 1 had CMV colitis and the other 2 had uptake of gallium in their colon. (Stool AFB's are not available at SFGH.) Only 1 patient had an abnormal CXR suggestive of pulmonary MAC disease (hilar adenopathy). 2 of these 5 patients received anti-tuberculosis (anti-TB) medications for 2 and 5 weeks prior to their dissemination. The 11 patients without evidence of dissemination had follow-up with negative AFB blood cultures of 31-442 days (median 112 days). 6 of these 11 patients received anti-TB meds (range; 2-8 months, median; 6 months). Only 2/11 complained of diarrhea and none had known intestinal pathogens. Only 1 patient had an abnormal CXR suggestive of pulmonary MAC disease (cavitary lesions) which improved with anti-TB meds. In these 11 patients 7 had 10 repeat sputums for AFB. 2 of 3 patients treated with anti-TB meds had a positive repeat sputum culture for MAC. Overall, 6/10 repeat sputum samples were negative for any AFB. Dissemination of MAC is associated with diarrhea. Use of anti-TB meds is of uncertain value.

WP.218 Use of HPA-23 in Patients with AIDS: Observed Toxicity During an Eight Week Trial.
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As part of a multi-center phase I trial, the experimental antiviral agent HPA-23 (Heteropolyanion-23, or antimonio-tungstate) was given to 16 patients with CDC-AIDS (10 with Pneumocystis carinii pneumonia, 4 with cutaneous or oral Kaposi's sarcoma, one with both PCP and KS, and one with Candida esophagitis). Protocol required five daily intravenous injections per week, and lasted eight weeks. Four dosing levels were used (0.25, 0.5, 1, or 2 mg/kg/day) with four patients assigned to each level. Four patients did not complete protocol because of intercurrent illness (one had rapidly progressive KS and three required conventional antibiotic therapy).

The only immediate toxic reaction occurred upon extravasation of drug, on at least one occasion in each subject, and was characterized by rapid onset of pain followed by erythema and swelling around the injection site. Symptoms persisted for 3 to 5 days after extravascular injection, but there were no long term sequelae. Subjective side effects included a slight metallic taste noted by several patients and nausea and loss of appetite. The most consistent toxic effect was a decrease in platelet count which occurred in all twelve patients who completed protocol. Platelet counts (x1000): week 1: 193 ± 14 SEM, week 5: 124 ± 13 week 9: 97 ± 16. Marked leukopenia (< 2000) occurred in a few patients, but did not persist on continuation of HPA-23. Renal function remained unimpaired. Moderate elevation of transaminases did occur in the group receiving the highest dose. Overall, HPA was well tolerated in this group of 16 patients with AIDS.

WP.219 Topical Acyclovir for Treatment of Hairy Leukoplakia
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This is a double-blind placebo-controlled crossover study to test effectiveness of 5% Acyclovir ointment in controlling lesions or oral "hairy" leukoplakia (HL) in a group of immunosuppressed volunteers infected with HIV. HL was described by Greenspan, Greenspan, and Conant in 1985, and is characterized as a white, adherent, often filliform oral lesion found mainly on lateral tongue borders with characteristic histologic appearance showing fine keratin projections, koilocytosis of prickle cells, and little subepithelia inflammatory cell infiltration. There is evidence of Epstein-Barr virus in the epithelial cells. HL has been observed only in immunosuppressed individuals, a great many of whom are homosexual males, seropositive for HIV antibody. It is highly associated with progression to AIDS in these individuals. Treatment of lesions of HL is useful in relieving patient anxiety and removing lesions which might be confused with oral candidiasis.

Twenty subjects with clinically diagnosed HL applied ointment to lesions 5 times a day for 4 weeks (2 weeks ACV ointment, 2 weeks polyethylene glycol base placebo). Nystatin suppositories were dissolved orally twice daily during the month of treatment and candida cultures were done both before and at the completion of the study to eliminate confusion of HL with oral candida. Clinical evaluations, including photographs of the lesions, were done weekly. A beneficial effect of study medication ointment has been observed in some patients, suggesting that topical ACV may be effective in suppressing Epstein-Barr viral replication in these lesions.

WP.220 Treatment of Pulmonary Kaposi's Sarcoma with a Combination of Adriamycin, Vincristine, and Bleomycin.

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Pulmonary Kaposi's sarcoma (KS) in AIDS is a late manifestation usually diagnosed in patients with extensive cutaneous disease. In one series the median survival after diagnosis was 1.5 months. Between 7/85 and 1/87, 12 patients with extensive pulmonary KS were seen. Patients ranged in age from 23 to 61 years (mean, 38 years). 2 had received prior chemotherapy. There were 5 patients with B-symptoms and 2 patients with a prior opportunistic infection. All patients had extensive cutaneous and endobronchial involvement with KS, pulmonary symptoms, and negative gallium scans. Other problems included hemoptysis in 4 and serosanguineous pleural effusions in 2. The chemotherapy regimen consisted of Adriamycin 50 mg IV on day 1, Vincristine 2 mg IV on days 1, 8, and 15, and Bleomycin 15U IV days 1 and 15 of a 28 day cycle. All patients received dapsone 25 mg po qid as prophylaxis for PCP. 6 patients initially received a reduced dose of Adriamycin because of leukopenia. None had a measureable response and the mean survival was 1.5 months. In contrast, all 6 patients who received the full dosage achieved greater than 75% clearing of their pulmonary infiltrates, resolution of their pulmonary symptoms, and had a mean survival of 10 months (range 7 to 12). 4 of these patients required a reduction in the dose of Adriamycin after 3 to 7 cycles because of leukopenia. Progressive pulmonary KS appeared within 3 months in these patients. To date, 10 patients have died, 9 of pulmonary KS and 1 of sepsis. No patients developed an opportunistic infection. Toxicity included mild myelosuppression, moderate alopecia, and mild nausea and vomiting in all patients. Our results indicate that this regimen is effective and well tolerated in the subset of patients who have adequate bone marrow reserve.

WP.221 Major Opportunistic Infections in AIDS Patients after More than Eight Weeks of Azidothymidine (AZT) Therapy.

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This report examines the frequency, types, and outcomes of AIDS-defining opportunistic infections (OI's) in patients treated with AZT for more than 8 weeks. Twenty-two patients with previous Pneumocystis Carinii pneumonia (PCP) were enrolled in our study. Nineteen of the 22 completed more than 8 weeks of AZT therapy. Eleven patients were treated with 250 mg every 4 hours for 10-12 weeks and then 200 mg every 4 hours thereafter. The other 8 patients were treated with 200 mg every 4 hours. AZT was discontinued or reduced to 100 mg every 4 hours if patients developed granulocyte counts of <750 or platelet counts <50,000.

Eight of 19 patients (42%) developed recurrences of PCP. These infections were documented between weeks 10-24 after starting AZT. Most of these recurrences were mild as measured by febrile days, arterial oxygen tension, and length of hospital stay; two of five tested had negative lung gallium scans. However, fatal complications developed in 2 of the recurrent PCP patients, one from respiratory failure due to PCP and another due to severe candida esophagitis, aspiration pneumonia, and lung abscess. Two patients developed cryptococcal meningitis at weeks 12 and 20; one died. One patient, at week 24, developed peri-rectal herpes simplex ulcerations which persisted > 1 month despite concurrent acyclovir therapy. In summary, 12 out of 19 patients (63%) developed major OI's after week 8 of AZT therapy. Three of these OI's were fatal. While AZT therapy may decrease the incidence of OI's initially, such OI's continue to occur and can result in fatality.

WP.222 Blood Levels of Pentamidine in AIDS Patients (Pts) Receiving Monthly Prophylaxis

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Pneumocystis carinii pneumonitis (PCP) recurs in 20 to 70% of AIDS pts; most are unable to tolerate prolonged oral TMP/SMX prophylaxis. Pentamidine prophylaxis is appealing because of its prolonged tissue half-life, but the pharmacokinetics in pts receiving intermittent doses is not known. Preliminary studies indicate a decrease in PCP recurrences with monthly pentamidine prophylaxis.

Eight pts receiving monthly intravenous infusions of pentamidine at a dose of 4 mg/kg were studied. All had received previous pentamidine therapy for PCP (avg. total 3338 mg), and all had at least one dose of prophylactic pentamidine (avg. 5.6 doses) before blood levels were determined. The average cumulative prophylactic dose was 1526 mg. An HPLC assay with a sensitivity limit of 2.29 ng/ml was used to determine peak and trough pentamidine blood levels. Levels were performed 2 or 3 times for each pt.

In 6 of 8 pts trough blood levels were consistently detected; one pt never had detectable trough levels and another had intermittently detectable levels. Peak blood levels averaged 949 ng/ml (range 130-2612 ng/ml). The presence of detectable trough levels and the magnitude of the peaks did not correlate with the cumulative dose. Two of the 8 pts had recurrent PCP; one had discontinued pentamidine prophylaxis when AZT treatment was initiated, and one other was terminally ill with disseminated MAI infection and Kaposi's sarcoma.

Detectable blood levels of pentamidine are present for at least one month after a 4 mg/kg intravenous dose in AIDS pts who have received previous therapy with pentamidine. Further studies of the pharmacokinetics of intermittently administered pentamidine are in progress.

WP.223 Improvement in HTLV-III/LAV-Associated Dementia and Neuropathy Associated with Administration of 3'-Azido-2',3'-Dideoxythymidine

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Neurological manifestations of HTLV-III/LAV infection are increasingly being recognized as an important clinical problem and, as has been shown by Drs. Shaw, Gallo, and coworkers, the brain is a major site of replication of HTLV-III/LAV. Based on these findings, we have administered 3'-azido-2',3'-dideoxythymidine (AZT) to 7 patients with HTLV-III/LAV-associated neurological disease: 4 with dementia, 2 with peripheral neuropathy, 1 with both dementia and peripheral neuropathy, and 1 with a T10 paraplegia. Levels of AZT in the cerebral spinal fluid 4 hrs after a dose were 55% of simultaneous plasma levels. By 3 to 8 weeks after being started on AZT, each of the 6 patients with dementia and/or peripheral neuropathy had improvement in neurological dysfunction as assessed by examination, neuropsychometric testing, and/or nerve conduction studies. In particular, patients with dementia had substantial improvement in Trailmaking, Weschler memory, and pegboard tests. The patient with T10 paraplegia, however, did not improve. One patient whose dementia improved was studied by positron emission tomography (PET). At the start of therapy, he had a heterogeneous pattern of glucose metabolism with relative decreases in the posterior temporal, occipital and thalamic regions; a repeat PET scan after 13 weeks had become more normal. In 2 of the patients the improvement seen was transient, and they expired from pneumonia after 6 to 8 months of therapy; the other 4 patients who improved continue to do well after 2 to 16 months of therapy. These results suggest that certain HTLV-III/LAV-associated neurological abnormalities are reversible following the administration of anti-retroviral chemotherapy and they provide a rationale for a larger study in patients with this disorder.

WP.224 Longterm Treatment of Severe AIDS and ARC Patients with Oral Ribavirin: A Pilot Study

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A Phase I Study of oral Ribavirin (RBV) for 8 weeks (Dec-June 1985-86) in 10 AIDS and 5 ARC patients showed suppression of HIV in blood, enhanced lymphoproliferative response to lectins and fewer opportunistic infections on RBV. On stopping drug, HIV was again detected in blood (Crumpacker et al., Proc. 2nd Int. Conf. on AIDS, Paris, 1986, p. 34). To determine if prolonged use of RBV would enhance survival, 5 AIDS patients and 3 ARC patients who had survived the 8 week trial of oral RBV were enrolled in a study of continuous RBV at 600 mg/day in July 1986. AIDS patients had PCP as their initial opportunistic infection, had T4 cells less than 100/mm^3 (mean=30/mm^3) and none had KS at start of Rx. From July-Feb 1987, no patient has had recurrent PCP, and 6 of 8 are surviving. (In a comparable untreated group of 10 AIDS patients followed at BIH, 7 developed recurrent PCP in a mean time of 6.5 months.) Two AIDS patients died after 4 months on RBV with progressive AIDS encephalopathy, but no other infections were found. In 8 patients, 4 AIDS associated events occurred: 3 episodes of CMV retinitis (2 in 1 patient) 1 episode of candida esophagitis and 1 new KS lesion. In 3 ARC patients, one developed CMV retinitis to progress to AIDS. In the AIDS patients, initial clearing of HIV with RBV and enhanced lymphoproliferative response to lectins was associated with prolonged survival. Mean survival time from initial diagnosis of AIDS with PCP is 18.5 months (as of 2-1-87) in the 5 AIDS patients on prolonged RBV. RBV is well tolerated as 4 patients have required no transfusions and 4 have required 2 units of packed RBV/per month to maintain HCT=30. This pilot study of prolonged oral RBV in severe AIDS patients shows that RBV is well tolerated, associated with prolonged survival and fewer opportunistic infections.

WP.225 Transplantation of Thymic Tissue to Reconstitute the Immune System of Patients with AIDS

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Thymic epithelial fragments were transplanted into 15 patients in an advanced stage of the acquired immune deficiency syndrome (AIDS). One patient was given interleukin 2 in addition to thymic tissue. We demonstrated the following : (1) Thymic epithelial fragments cultured before transplantation to remove T cells survived for months after transplantation in 8 of 15 patients and seemed to be responsible for a partial, selective, but transient repopulation of the circulating T cell pool. (2) The absolute number of T8 cells, but not T4 cells, increased three to four weeks after the procedure in eight of the fifteen subjects. (3) This increase in T8 cells was associated with clinical improvement and increased T cell responsiveness in vitro in some cases. In one case a severe bilateral retinitis thought to be due to cytomegalovirus (CMV) cleared spontaneously, a development unique in our experience with patients with AIDS. Improved control of tuberculous infections was noted in two cases. The clearance of resistant pneumocystis carinii pneumonia and a cessation of previously intractable diarrhoea in two patients coincided with engraftment. (4) Thymic tissue transplantation as a single therapeutic manoeuvre is unlikely to reconstitute the immune system of patients with AIDS, but the potential of the approach, used in combination with agents that block replication of human T cell lymphotropic virus type III deserves further study.

WP.226 Evaluation of HIV Antibody Reactivity in Blood Donors with Atypical Western Blot Patterns

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Blood donors reactive for HIV antibody by ELISA who showed atypical patterns on Western blot (WB) representing several patterns of core protein reactivity (p15/p17, p15/p17 and p55, p24, p24 and p55, p15/p17 and p24) were followed for 2-10 months. Characterization of these antibodies was performed by 1) use of recombinant HIV proteins and synthetic peptides, 2) determination of cross-reactivity to HTLV-I, HTLV-II, HTLV-IV, 3) assessment of immune status and potentially interfering auto-antibodies. All but two donors maintained the same HIV core protein antibody reactivity throughout the follow-up period; one showed a diminished pattern; the other became fully antibody positive. Eighteen of 20 donor sera showed clear core reactivity with GAG-55 HIV recombinant protein. Ten of 19 donors' samples demonstrated cross-reactivity to HTLV-IV; three of these 10, in addition, cross-reacted with HTLV-I. Immune status of all donors was normal, but rheumatoid factor was detected in 2 of 20. Thus our evidence so far strongly suggests that the atypical WB reactivity observed is directed against retroviral core proteins. As part of this study, donors were questioned during the follow-up visits. On interview, three donors reported possible risk factors for HIV infection that were not acknowledged at the time of donation. Based on these results, we conclude further study of donors with this "atypical" reactivity is warranted. As an interim measure blood identified by screening tests which detect antibodies reactive with core proteins should not be transfused.

WP.227 Low Dose Naltrexone in the Treatment of AIDS

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Thirty-nine patients, 38 with CDC defined AIDS and 1 with ARC were treated with 1.75 mg. qhs of naltrexone, an oral opiate antagonist, in a double blind placebo controlled study. The naltrexone group showed a significant drop in pathologically elevated levels of serum alpha interferon compared with the placebo patients ($p < .01$). The double blind phase was ended at 3 months, and placebo patients were given naltrexone. Of 39 patients on naltrexone, 23 showed a marked decline in alpha IFN levels (from means of 144 i.u. to 11 i.u.) over a 12-month period. Sixteen patients showed sustained alpha IFN elevation. Accordingly, a patient classification of responder vs nonresponder was established. During the course of the study, the 23 responders experienced significantly less O.I's than the 16 nonresponders ($p < .01$). There were 8 O.I.'s in the responder category and 19 O.I.'s in the nonresponder category. Of the 8 O.I.'s in the responders, 4 were mild episodes of P.C.P. Three of these 4 episodes occurred before the patient's alpha IFN level had decreased from the admission level. All of the other 23 O.I.'s in both groups were life threatening and in fact, 17 were fatal. In addition to the significantly higher rate of O.I. occurrences in the nonresponder group, there was also a significantly higher death rate. As of December 17, 1986 there were 13 deaths (81%) in the group of 16 nonresponders and 4 deaths (17%) in the group of 23 responders ($p < .01$). No side effects were noted.

WP.228 Response to therapy in 50 patients with HIV-related thrombocytopenic purpura.

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Fifty adults (43 males and 7 females) with serum antibodies to HIV were treated because of profound chronic thrombocytopenia with clinical bleeding in all but two cases. These patients included 25 intravenous drug addicts, 22 homosexual men, 2 transfused patients and 1 hemophiliac. None had full blown AIDS ; 20 had persistent generalized lymphadenopathy and 5 splenomegaly.

Mean (± SE) platelet count was $14 \pm 2.10^9/l$ (range 2 to 48). Thirty of 40 tested patients had elevated platelet-bound IgG levels and 11 of 23 had antiplatelet serum antibodies. Lymphocyte count was below 1 500/mm^3 in 28 patients and T4 cell count below 400/mm^3 in 20 of 46 patients.

Prednisone (1 mg/Kg/day for at least 1 month) was given to 31 patients. A response occured in 19 cases with platelet count $> 100.10^9/l$ in 9 and $> 50.10^9/l$ in 10 others ; 6 patients sustained their response off steroids. Three of 21 patients responded to danazol therapy (600 mg/day for 6 weeks). Fifteen of 21 patients receiving high dose intravenous IgG (0.4 g/Kg/day for 5 days) responded and 6 of them could be maintained upon repeated boosters. Nine patients received anti-Rhesus immunoglobulin infusions (1 000 µg/day for 2 days of anti-D IgG in 7 Rh+ patients or anti-c IgG in 2 Rh- patients. A partial response occured in 6. Splenectomy was performed in 20 patients and was successful in 16. In our experience, it was the best treatment for patients with severe and symptomatic thrombocytopenia. During a mean follow-up of 16 months (range 4 to 46) one patient developed AIDS (15 months after the diagnosis of thrombocytopenia).

WP.229 IMMUNOMODULATION with BESTATIN in a Double-Blind Controlled Trial with HIV-positive Homosexual Men.

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Bestatin has previously been used to stimulate the cell mediated immune response in immunodepressed cancer patients. In this study we investigated the effect on immunological, haematological and biochemical variables in HIV-positive homosexual men.

22 subjects with PWM <50% of normal and/or T-helper cell count $< 0{,}6\ 10^9/l$, but without any opportunistic infections according to the CDC definition of AIDS were treated with bestatin capsules 60 mg daily or placebo for 4 weeks.

The immunomodulating effects were evaluated by lymphocyte transformation tests, T-cell subsets, natural killer cell activity, in vitro alpha-interferon production, change in HIV antigen titre and basophil histamine liberation.

Values were measured before treatment and 4 weeks and 10 weeks later.

Full results will be presented at the conference.

WP.230 Gastrointestinal (GI) Non-Hodgkin's Lymphoma (NHL) in Patients (pts) at Risk for Acquired Immunodeficiency Syndrome (AIDS)

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At our institution 89 cases of diffuse aggressive NHL occurred in AIDS-risk pts since 1981. Of these, 15 male pts (14 homosexual, 1 IVDA) were diagnosed (dx) with GI NHL. Pathologic type was diffuse large cell, immunoblastic plasmacytoid (6) and diffuse large cell noncleaved (9) or by Rappaport classification diffuse histiocytic lymphoma (15). Concurrent CMV was evident in 2 biopsies and Kaposi's sarcoma (KS) in one other. Median age was 37 years (31-45). 5 pts (33%) had prior AIDS (3 opportunistic infection (OI), 2 KS) and 10 pts (67%) had NHL as their initial manifestation of AIDS. Of the latter 10, 5/5 were (+) for HIV antibody. Of the 5 not tested, 2 had prior ARC and 3 were only known to be in an AIDS-risk group. 4 pts (27%) had a concurrent OI at dx of NHL. Sites of primary disease were stomach (3), small bowel (6), large bowel (1), rectum (2) and perirectal mass (3). Median LDH at dx was 303 (164-1521). Clinical staging showed: Stage I - 8 pts, Stage II - 2 pts, Stage III - 2 pts and Stage IV - 3 pts. 12/15 had B symptoms. Treatment (rx) of pts has varied including surgery and combination chemotherapy (3), combination chemotherapy alone (8), surgery alone (1) or radiation therapy (1). Median survival is 16 weeks (w) with 8 pts dead, 6 alive (7,8,16,17,18,27 w) and 1 lost to follow up. Because of the individualized nature of rx regimens employed, no overall conclusion can be drawn regarding response to rx. In conclusion, GI NHL occurs in a subset of AIDS-risk pts as their initial dx of AIDS presenting as local regional disease. NHL should be considered in AIDS-risk pts with abdominal/rectal symptoms or GI ulcers even with documented OI or viral GI infection. Despite its early stage at presentation, this subset of extranodal NHL has a poor prognosis and warrants aggressive rx.

WP.231 Oral Ganciclovir: Human Pharmacokinetics and Tolerance

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Ganciclovir (DHPG, BW759U) is a nucleosida analog which inhibita herpes viruses in vitro, and which has been effective in treating severe cytomegalovirus (CMV) infection in immunocompromised patients. To date, the drug has been administered only intravenously. As most patients with AIDS and severe CMV diseaae have required lifelong daily suppressive ganciclovir (GCV) therapy to control disease progression, oral therapy would appear to have practical advantages. We studied the pharmacokinetics of orally administered GCV in 4 patients with AIDS and CMV retinitis. Repeated oral GCV doses (10-20 mg/kg every 6 hours) were well-tolerated. With a 10 mg/kg dose given every 6 hours, mean steady-state peak (Cmax) and trough (Cmin) plasma levels were 2.01 uM and 0.87 uM, and the AUC_{0-24} was 33.6 uM.hr. With a 20 mg/kg dose given every 6 hours, mean Cmax and Cmin were 2.96 uM and 1.05 uM, and the AUC_{0-24} was 47 uM.hr. Based on urinary excretion and blood levels, calculated absorption was 4.5% of the 10 mg/kg q 6 hour dose and 3.0% of the 20 mg/kg q 6 hour dose.

The low blood levels achieved make it unlikely that oral GCV therapy will be effective for acute treatment of CMV infections. Mowever, with the 20 mg/kg dose, the mean Cmax excaeded the ED_{50} of most clinical CMV isolates, and the mean Cmin level was 5 times higher than that typically obtained with daily intravenous GCV maintenance therapy. Despite its limited bioavailability, orally administerad GCV should be studied to determine whether it will be useful for long term suppressive anti-CMV maintenance therapy in AIDS patients with severe CMV disease.

WP.232 The efficacy of stress management in reducing high risk behavior and improving immune function in HIV antibody positive men.
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This study was conducted to test the hypothesis that stress management training for HIV antibody positive men would result in (1) lower stress and depression, (2) decreased high risk sexual behavior, and (3) improved immune function. Sixty gay men, who were positive for antibodies to HIV but otherwise healthy except for lymphadenopathy, were randomized to treatment of wait-listed control groups. Treatment Ss were given an 8-week stress management program which included training in the relaxation response, strategies for coping with being antibody positive, strategies for coping with relationships, strategies for coping with common stressors, and motivation for health habit change. Dependent measures included scales to assess stress and depression, reports of sexual behavior during the month prior to assessment, WBC, T-Helper and T-Suppressor enumeration, and measures of immune function(NK Activity, Lymphocyte Response to Mitogens, Lymphocyte proliferation to antigen). The stress management intervention was effective on several dimensions. We found no differences between treatment groups at baseline. At posttest, the treatment group reported significantly less stress and depression than control Ss. Treatment Ss also reported significantly lower rates of sexual behavior capable of transmitting HIV. We also found significantly higher levels of NK activity and response to mitogen in the treatment Ss.

WP.233 Inactivation of the Human Immunodeficiency Virus by Neutral Buffered Formalin and Quaternary Ammonium Compounds.
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Because persons working in pathology laboratories have expressed concern about the survival of the human immunodeficiency virus (HIV) in tissues fixed with 10% neutral buffered formalin (NBF), we evaluated this reagent's effect on HIV survival. HIV preparations (LAV prototype strain) with ID-50 titers $\geq 10^5$ were rendered undetectable in the ID-50 assay by treatment with 1% (1% NBF = 0.37-0.4% formaldehyde) or greater NBF. We also tested effects of quaternary ammonium coumpounds (quats) on virus viability. The three quats tested--a double quat, a twin-chain quat and a single chain quat--either alone or in combination constitute virtually all commercial products marketed in the United States. In our test system all quats were capable of inactivating HIV (effective concentrations ranged from 500 to 1000 ppm) further demonstrating HIV's sensitivity to a spectrum of disinfectant chemicals.

WP.234 Development of a Simple Clinical Method to Screen for AIDS Virus in Blood Donors in Underdeveloped Countries.
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A low-cost clinical method for determining AIDS virus (HIV) positive blood donors is needed to control the spread of AIDS via blood transfusions in underdeveloped countries. In many areas of the world cost precludes the use of antibody screening tests. Using a San Diego population of 159 healthy gay men of whom half were HIV antibody positive, three simple clinical tests were used in a logistic model to detect seropositive men: hematocrit, number of enlarged (>1 cm) cervical lymph nodes and number of non-inguinal regional sites with enlarged lymph nodes.
This 3-factor model yielded a test with 91% sensitivity and 62% specificity. Addition of more expensive or more complicated predictors made only slight improvement in test performance. A simpler model which excluded hematocrit and utilized only the examination of lymph nodes maintained sensitivity (90%), but was less specific (42%) and thus, would exclude more uninfected donors. Even at the high seroprevalence (18%) currently reported in blood donors from some African cities (Lancet 1986;ii:1113), the predictive value of a negative test for the 3-factor model is 97% and for the 2-factor model is 95%. Deployment of these tests requires that they first be validated in the population in which they are to be used because sensitivity and specificity of the test may differ between populations and observers. We conclude that a simple, low-cost clinical exam may provide a means to screen blood where cost precludes use of currently available antibody tests.

WP.235 Summary of a Statewide Program to Identify Blood Donors Infected with Human Immunodeficiency Virus (HIV): Minnesota, USA.
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HIV antibody screening (with Western blot confirmation) of blood donors began in March 1985 in Minnesota. Follow-up of infected donors can provide useful public health information. We report here the results of a statewide program sponsored by the MN Dept. of Health to identify HIV-infected donors. Approximately 400,000 donors have been screened in Minnesota for HIV antibody. To date, 15 state residents who have antibody to HIV have been identified. 14 are male and 1 is female. The mean age is 30 years (range, 20 to 39). 36 patients in Minnesota received blood from previous donations from these donors; 3 of 15 recipients without other risk factors (20%) were determined to be HIV antibody positive (14 others are known dead and 7 have not been contacted). To date, interviews have been completed for 12 donors (all male). Risk factors were identified for 11: 10 are homosexual or bisexual, and 1 had sex with a female prostitute. For homosexual or bisexual men, the mean number of male sexual partners since 1977 is 20 (range 1 to 50). When asked why they had donated blood, 8 indicated that they did not perceive they were at risk for acquiring HIV infection, 2 felt peer pressure to donate blood and 1 wanted to know his HIV antibody status. Our results indicate that most HIV antibody positive blood donors in our state have known risk factors for acquiring infection and that lack of (or denial of) perceived risk is the major reason that persons in high-risk groups continue to donate blood.

WP.236 Confirmation of Antibodies to HIV Prior to Donor Notification of Test Results: The New York Blood Center Approach.
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Despite improvements in the specificity and sensitivity of ELISA screening assays for antibodies to HIV, high frequency of false positives warrants performance of additional assays prior to donor notification. The most accepted is the Western blot (WB), a research test without uniform criteria for interpretation which in some instances produces uninterpretable results.
We have found strong positive correlation between WB positivity and absorbance in the ELISA assay for two commercially available tests. WB positivity is low at low ELISA absorbance ranges and approaches 100% at high ranges. However, some samples are WB positive in the low range, and others are negative in the high range. To address these inconsistencies we used additional assays such as the indirect immunofluorescence (IFA) and ELISA based on different antigenic preparations.
Analysis of results generated a decision tree for confirmatory assays: (a) WB negative in the low absorbance range or positive in the high absorbance range is accepted as a true result; (b) all other samples are subjected to additional confirmatory assays.
The majority of the individuals found to be antibody positive returned for test repeat, notification and counselling. Results indicated that the initial decision was correct in all cases. Studies of helper and suppressor T cells showed that 60% of these individuals had ratios below one, suggesting alterations of immune function.

WP.237 Looking Forward: The Challenge of Lookback
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The vast majority of high-risk donors self-excluded prior to anti-HIV test licensure, and thus are not presenting to blood banks and triggering lookback. This is evidenced by extrapolation from the progressively declining seroprevalence rate over the first two years of the testing (0.3% to 0.03%), and our experience with an expanded lookback effort. As of January, 1987, prospective screening has identified 32 HIV-positive donors with prior donation histories, which has resulted in notification of only 200 potentially exposed recipients. Our broader program has been triggered by two additional events: active identification of reported AIDS patients with a history of donation, and active investigation of reported transfusion-transmitted HIV infections. Of 139 AIDS patients who donated blood at Irwin Memorial Blood Bank since 1977, only 10% were reported as such by local health departments; the remainder were identified by active cross-referencing of AIDS case listings with donor records. These 139 AIDS patients donated blood to ca. 950 people (53/106 tested recipients are HIV+), 28 HIV+ high-risk donors found while investigating 50 TAA cases has led to notification of an additional 322 potentially infected recipients thus far. Recipient testing of each group showed that 50% of traced recipients were infected. Although our broader lookback efforts result in 7 fold greater notification over standard programs, it is unlikely that even this program is tracking the majority of exposed recipients.

WP.238 CLINICAL OUTCOME OF HIV INFECTION IN HAEMOPHILIA
UNI. DEPT OF MEDICINE GLASGOW ROYAL INF SCOTLAND.

RAJAN MADHOK JA GRACIE GDO LOWE CD FORBES

The outcome of HIV infection in Haemophilia is not clear. One US study showed a 13% 3 yr. incid. of AIDS (SCIENCE 231992-5). No similar studies are available from elsewhere. We report on the clinical immunological outcome of 23 HIV antibody positive haemophiliacs followed since seroconversion mean :49.5 mths range 24-66. One patient is lost to follow up but is known to be alive.

No patient has developed AIDS but 1 Pts. has had recurrent bacterial infections. 1 pts. oral candida. Specific manifestations of HIV infection include thrombocytropenia in 1 pts. episodic lymphadenopathy in 3 pts.

The total lymphocyte cnt fell over 3 yrs. All pts. had a T4 lymphopenia median 423 range 321-734. The T4 cnt in early seroconverters ($\geq$ 50 mths.) was no different from late seroconverters but in individual pts. th T 4 cnt fell significantly ($p \leq 0.05$ prd WX test). The results of this cohort confirm the previous finding of a lower risk of AIDS in haemophilia. (SCIENCE 231 992-5) relative to other risk groups. Factors other than time may influence the decline in T4 cell numbers.

WP.239 Immunological Alterations Unrelated to HIV Infection in Transfused Children with Sickle Cell Disease

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Immunological abnormalities similar to those seen in AIDS have been reported in adults and children with sickle cell disease (SCD) receiving chronic RBC transfusion. The extent to which these abnormalities develop in the absence of HIV infection is unknown. We have performed longitudinal serological and immunological evaluations of 20 transfused children with homozygous SCD from 1983 to 1986 to determine the frequency of immunological alterations over time. Seven children (2-16 years) receiving sporadic transfusion (STX), and 13 children (9-16 years) receiving chronic transfusion (CTX) were studied.

The mean numbers of transfusions received prior to the first assessment of the STX and CTX groups were 5.9 and 90.7 respectively. The second assessment was done from 25 to 44 months following the first. The groups received a mean of 4.S and 79.7 transfusions respectively during the study interval.

No correlation was observed in either group between the transfusion load and OKT3, OKT4, or OKT8 numbers, OKT4/OKT8 ratio, and serum levels of total Ig or beta-2 microglobulin. Four of the I3 STX children experienced absolute OKT4 reductions of greater than 8S% over the study interval. Three of the seven CTX patients experienced absolute T4 reductions of greater than 50%. All other children remained normal. One CTX patient with a 51% reduction in T4 count seroconverted to HIV. All other patients were HIV-EIA negative, although four demonstrated reactivity to HIV/p24 by Western blot. Our data suggest that no consistent immunological abnormalities are produced by large numbers of RBC transfusions over time, but that T4 lymphopenia not directly attributable to HIV may occur in selected children .

WP.240 THE EFFECTS ON THE DONOR BASE OF A NATIONWIDE SCREENING PROGRAM FOR THE PREVENTION OF TRANSFUSION ASSOCIATED HIV INFECTION

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Maintaining an inventory of the safest possible blood and components while maintaining an adequate donor base has been a continuing challenge ever since the possibility of transmission of AIDS by blood was recognized. Through the implementation of nationwide, standardized donor and donation screening procedures the Canadian Red Cross has, however, been able to essentially eliminate the threat of HIV infection through transfusion with no significant impact on the donor base. Donor screening includes obligatory reading of an information pamphlet, individual interviews with options to exclude use of possibly infectious units, laboratory testing of donations by enzyme immunoassay (EIA), discard of repeatably EIA reactive donations, and confirmatory testing by Western blot (WB). Donors are forewarned that a positive test means that they will be permanently deferred from donating, that they should consult their doctor and that, where required by law, their anti-HIV status will be reported to regional health authorities. Nevertheless, donations during the first year of anti-HIV testing increased over the preceding year by 2%. The incidence of repeatably reactive donations was 0.3% and some 95.6% of these could not be confirmed by WB. A follow-up study of those who return to donate is underway. Preliminary analysis of 377 returnees shows 47.5% tested EIA-/WB-, 34% remained EIA+/WB-, 18% tested WB indeterminate and 0.5% had seroconverted to EIA+/WB+. A policy for notification of donors who consistently test EIA+ and/or WB indeterminate is under development. The data and findings outlined above will be updated on the basis of 1½ years experience at the time of presentation.

WP.241 HIV Positivity: The Psychosocial Impact of Donor Notification

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We began to notify and counsel donors with confirmed positive HIV antibody results in July 1985. In our experience, although the majority of donors from whom a reliable history could be obtained readily admitted to being in a known risk group for HIV infection, 24% denied any history of exposure to HIV. 43% of confirmed positive female donors and 18% of males were thus classified as risk "unknown."

All counseled HIV positive donors are invited to participate in a prospective natural history study of HIV infection in blood donors. As part of this study, we administer the Center of Epidemiologic Studies Depression Scale (CES-D Scale). This scale is a self-administered questionnaire designed to detect both the presence and the degree of depression in study participants. Questions address both affective and physical symptoms. Overall scores range from 0 to 60, with a score of greater than or equal to 16 indicative of clinical depression.

CES-D data is presented for the first 48 HIV positive donor subjects, as performed within two months of notification of their serologic results. 38 successfully completed all questions, and 45% had scores $\geq$ 16. Donors who acknowledged risk activity of HIV infection had higher scores (mean = 21) then donors who acknowledged no risk (mean = 13) ($p < 0.1$).

We conclude that broad denial mechanisms exist in donors who deny risk for HIV infection. These mechanisms are intact not only when they donate blood but also when they are confronted with evidence of infection. Such denial will complicate donor notification, counseling and recommendations for behavior modification to prevent further transmission of HIV in this population.

WP.242 Diagnosis of HIV Exposure With a Competitive Enzyme Immunoassay (CIA) for Antibody to the Transmembrane Envelope Glycoprotein (gp41) of Human T-Lymphotropic Virus, Type III (HTLV-III).

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Conventional ELISA techniques have proven extremely useful in removing HIV infectious units from the blood supply. We have developed a specific and sensitive two-step competitive immunoassay (CIA) that utilizes a recombinant DNA derived full length p41 protein and a monoclonal antibody to detect antibodies to the transmembrane envelope glycoprotein (gp41). To show the reliability of anti-gp41 as an indicator of HTLV-III (HIV) exposure, we tested sera from patients with acquired immunodeficiency syndrome (AIDS), AIDS related complex (ARC), asymptomatic patients, and blood donors that were identified as seropositive by conventional screening ELISA and by Western blot. All samples tested were reactive using the recombinant p41 based CIA. To quantitatively compare sensitivity between Western blot and CIA, serial 2-fold dilutions of eleven patient sera (5 AIDS, 3 ARC, 3 asymptomatic) were tested. The CIA proved to be three to six 2-fold dilutions more sensitive than Western blot when scoring for gp41. In addition, early antibody response to HIV in seroconversions was detected by the CIA in samples nonreactive or weakly reactive with conventional screening tests and/or Western blot. These data indicate that antibody to gp41 is a highly reliable and consistent marker for HIV exposure throughout all stages of the disease.

WP.243 HOW SAFE WAS (AND IS) BLOOD TRANSFUSION IN SYDNEY, AUSTRALIA.

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72 cases of post-transfusion HIV infection in patients other than haemophiliacs have been reported and or traced by the Blood Transfusion Service in Sydney to the end of January 1987. 20 of these patients have developed AIDS (18 deaths), 14 have lymphadenopathy, the remainder have no symptoms. HIV infection has resulted from transfusion of whole blood, red cells, platelets and plasma. Follow-up studies have shown an extremely high risk of HIV transmission from all donations made subsequent to implication of that donor in a known case.

The number of donors who have been proven anti-HIV positive in look-back studies to date stands at 27; 18 of them have been responsible for transmission of the virus in 32 cases.

The risk of HIV infection increased progressively from 1 to 85,000 per unit transfused in 1980 to 1 in 4,000 in 1984. No case has been reported in patients transfused since routine screening for HIV antibodies commenced in Australia on 1 May 1985.

WP.244 Comparative Detection of anti-HIV in a Seroconverting Blood Donor

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Plasma drawn from a male homosexual at weeks 0, 9, 12, 15, 17, 18, 19, 20, and 23 (1981) was tested (1987) for anti-HIV by seven FDA licensed ELISA procedures, an unlicensed ELISA (Abbott: Envacor), Western Blot (WB), and IFA, as well as for HIV antigens by an experimental antigen-capture assay (Electro-Nucleonics), and for antibodies to H-9 cellular antigens.

One licensed ELISA procedure (Organon Teknika: Bio-EnzaBead HTLV III) detected anti-HIV at 12 weeks; the other six first detected anti-HIV at week 15. Signal to cutoff (s/co) ratios consistently increased following initial reactivity. With Envacor, anti-gp41/160 was detected at 12 weeks; anti-p24/55 at week 18. By WB, anti-p24 first appeared at week 15, followed by anti-gp41 at week 18; anti-p31 was never detected. With IFA, the 15 week and subsequent specimens were reactive. Antigen-capture assay detected HIV antigens at week 12 only; antibodies to H-9 antigens were never detected.

These data suggest 1) in anti-HIV seroconversion, HIV antigens are transiently serologically detectable, suggesting the presence of infectious virus, 2) anti-HIV can be detected by sensitive ELISA concomitantly with the first detection of HIV antigens, obviating the need for HIV antigen tests in current blood bank screening, 3) repeatably positive ELISA reactions with IFA/WB negative or WB p24 positive only results may represent early seroconversion; thus, follow-up studies are essential, 4) in sequential samples, consistently increasing s/co ELISA ratios, positive IFA results, and the emergence of antibodies to additional HIV antigens in WB are indicative of seroconversion, thus confirming infection, 5) current ELISA procedures have end-point sensitivities equal to IFA and WB, except Bio-EnzaBead which appears slightly more sensitive.

WP.245 Importance of T Cell Subset Determinations in Heavily Treated, Severe Hemophiliacs

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A retrospective study was undertaken to determine correlation between T cell changes and clinical outcome of patients with severe A or B hemophilia. 186 patients were followed from 1983 through 1986 with serial determinations of lymphocyte subsets and white cell and platelet counts. The patients were arbitrarily assigned to two groups based on T4 cell counts: 46 with less than 400 T4 cells (Group 1) and 140 with more than 400 T4 cells (Group 2). Median follow-up times were 17 months for both groups. In Group 1, 10 (22%) developed AIDS, 13 (28%) developed ARC, and 46 (50%) remained asymptomatic. In Group 2, 9 (6%) developed AIDS, 11 (8%) developed ARC, and 120 (86%) remained asymptomatic. When data from the AIDS patients were separated from the groupings, median T-lymphocyte values were:

	NonAIDS		AIDS	p
	≤400 T4 Cells	≥400 T4 Cells		
Initial T4	297	693	322	0.01
Final T4	224	562	143	0.01

The relatively unchanging course of Group 1 subjects may indicate either a long incubation period prior to clinical disease or a relatively high resistance to clinical infection. Subjects who had relatively stable values tended to remain asymptomatic. The T cell counts of the AIDS subjects were characterized by a marked progressive decline. Therefore, serial declines in T cell subsets may be an early indicator of clinical disease.

WP.246 Evaluation Of HIV Antigens Obtained From Commercial Sources By The Western Blot Technique

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HIV antigen preparations consisting of disrupted virus particles are available from several commercial sources and have been used as antigens for detection of antibodies. In order to evaluate the relative concentrations of the viral proteins and purity of these preparations, the HIV proteins were separated by the Western Blot technique. The relative amounts of viral and non-viral protein were determined by protein staining and analyzed by reflective densitometry. Immunoreactivity to a panel of patient sera was measured by enzyme immunoassay of the WB strips. With many of the commercial HIV antigen preparations, the majority of the proteins did not migrate at positions corresponding to immunoreactive viral-specific proteins and glycoproteins. Large amounts of protein were found at 70,000 Daltons and/or less than 18,000 Daltons. With some preparations, these contaminants reacted with ELISA negative sera samples to give faint bands. With some preparations a weak non-viral band was also noted at a position corresponding to the viral major capsid protein p24. These contaminants could confuse interpretation of HIV negative sera. The amount of protein migrating at particular band position did not necessarily reflect the potential immunoreactivity. This was most evident for high and low molecular weight regions. The highly immunogenic gp160/gp120 were often barely detectable or non-existent in some preparations by immunoreactivity. These studies emphasize the importance of careful evaluation of the purity and immunoreactivity of each commercial HIV antigen by WB analysis for diagnostic and analytical purposes.

WP.247 Studies of Normal Donor Specimens Causing Various Reactivity Patterns in Sensitive Western Blot Assays.

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Western blot (Wb) has become a valuable technique for demonstrating the antibody fingerprint of a particular serum to the antigens of HIV. However, as has been recognized, there are many Western blot assays being used currently with variations in virus preparations, blotting techniques, reagents and incubation conditions, visualization techniques and standards for acceptability. Recent attempts to use a very sensitive Western blot test to evaluate specimens from the clinical evaluation of the improved Bio-EnzaBead HTLV-III ELISA test system indicated that there were normal donor specimens having a variety of reactive bands, primarily in the p17, p24, p53 and p66 regions. However, periodically there was some reactivity in the gp41 area, but the banding was more restricted and not the characteristically diffuse zone, and repeated runs of the same specimen would not yield reproducible detection of bands in the gp41 region. Two specimens that appeared to have this type of nonreproducible gp41 reactivity were analyzed with a sensitive IFA technique used by the San Francisco Department of Public Health (J. Wilber); both were nonreactive even at a 1:3 dilution. Adsorption of the sera with a T-cell line followed by Western blot showed elimination of reactivity; the major reproducible band seen is to the p24 region, and this was completely eliminated. These results would caution that the use of very sensitive Western blot tests for evaluation of normal donor specimens may require multiple blot tests and/or possible adsorptions in order to indicate significant reactivity in Western blot.

WP.248 TRACING OF SEROPOSITIVE BLOOD DONORS TO ASSESS THE PRESENCE OF RISK FACTORS

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Starting from 1983 National Health Services and blood bank associations made recommendation that members of risk group for AIDS should refrain from blood donation, to reduce the risk of infection associated to the administration of infected blood. Nevertheless after the availability of screening tests for anti HIV antibodies, person at increased risk for AIDS started to donate blood to have a ascertain their immunologic status versus HIV infection. In Latium Region screening of blood unit for anti HIV antibodies is mandatory starting from 1985. Prevalence of seropositivity, Western blot confirmed is .0006. To evaluate the risk factors of seropositive blood donors and compliance to the self-exclusion programmes all seropositive subjects from National Transfusion Center of Italian Red Cross were contacted. From March 1985, 89113 blood donors have been tested. 228 were repeatable seropositive to screening tests and 53 confirmed by WB. 42 out of 53 seropositive have been traced. Of These 5 (11.9%) were intravenous drug addicts (IVDA), 21 (50%) IVDA in the past, 6 (14.3%) partners of a IVDA, 1 (2.4%) homosexual and IVDA, 3 (7.1%) homosexuals, 3 (7.1%) promiscuous heterosexuals, 2 (4.8%) not Known risk factors. This result evidences that the alternative sites availability, free of charge in Italy, for anti HIV testing and predonation appeals to refraln from donatlng plasma and/or blood are not effective in dissuading subjects at risk. Mass campaigns and more extensive pre-donation counselling and medical examinations are needed to avoid the risk increase of transfusion associated infections.

WP.249 Prospective follow-up of transfusion-associated acute HIV infection

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To identify recipients during the acute phase of TA HIV infection, 4,725 donor samples, collected in Barcelona during the 2 months prior to routine screening, were tested for anti-HIV by EIA.Of the 4 units positive by EIA and WB, only 3 had been transfused to 4 recipients.Of these,2 were dead at the time of identification,1 could never be contacted and 1 has been prospectively followed since posttransfusion week 4. This recipient,a 54-year old woman who received 1 positive unit of PRCs during breast cancer surgery, is currently undergoing weekly plasma and lymphocyte-pheresis.Results on initial evaluation of HIV-antibody, HIV-antigen (using commercial kits) and T-cell subsets are shown in the table.

	WEEKS POSTTRANSFUSION							
	4	5	6	7	8	9	11	13
HIV-Ab EIA	1:2*	1:2	1:2	1:1	1:1	1:1	1:2	1:8
HIV-Ab WB p160	+	+/-	+/-	-	-	-	+	++
p41	-	-	-	-	-	-	+/-	+
p24	-	-	-	+/-	+	++	+++	+++
HIV-Ag EIA	+	-	-	-	-	-	-	-
T4 (cells/mm^3)	ND	ND	NA	213	850	452	926	983
T8 "	ND	ND	NA	2,671	1,175	1,006	964	1,109
T4/T8	ND	ND	NA	0.07	0.7	0.4	0.9	0.8

ND:Not done; NA:cells not available;*end-point dilution

No clinical symptoms or physical abnormalities have been detected during follow up. Attempts to recover the virus from cryopreserved lymphocytes and plasma,characterization of early morphological and functional changes in PBLs and search for neutralizing antibody in sequential samples are currently under way.

WP.250 Anti-HIV IgM Screening in High-Risk Subjects

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Most of the tests developed for the screening of HIV antibodies are aimed at HIV-IgG, only a few at HIV-IgM detection, while competition tests theoretically should be able to evidence both classes of immunoglobulins. Sixty-five parenteral drug-addicts (PDAs) and 123 polytransfused subjects, all resulting HIV-IgG negative by different commercially available tests, were investigated for the presence of HIV-IgM also by a modified ELISA method which we developed to make it more specific and sensitive for IgMs (Tech IgM HTLV III, Technogenetics, Torino, Italy). According to this 5 out of 65 HIV-IgG negative PDAs (7.7%) were found HIV-IgM (WB-IgM confirmed) positive; IgM positivity was also evidenced in 3 polytransfused, HIV-IgG negative subjects. IgM-IgG switch was shown in 4 out of 5 PDAs 1 to 38 weeks (mean 19 weeks) after the first IgM-positive result. In the 3 HIV-IgM positive polytransfused subjects, for each of whom an HIV-positive donor was traced, IgM appeared approximately 12 weeks after transfusion and, in 2 of them, IgM-IgG switch occurred after another 8 weeks. In all subjects examined, HIV-IgM, representing the earliest sign of infection, were detected by our test (WB-IgM confirmed) at least some weeks before this could be done by other methods, including competition tests.

THURSDAY, JUNE 4

Plenary Session V

TH.1.1 The Human Immunodeficiency Viruses: 1987.

Luc Montagnier, Institut Pasteur, Paris, France.

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

Virology—Related Viruses

TH.2.1 Nucleotide Sequence Analysis of the West-African AIDS Virus, HIV-2.

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A novel retrovirus, the human immune deficiency virus type 2 (HIV-2, previously named LAV-2), was isolated from patients with AIDS and related conditions originating from West Africa (Guinea Bissau, Senegal, Gambia, Ivory Coast ...). This virus is related to HIV-1, the causative agent of AIDS in Central and East Africa, as well as the USA and Europe, by its morphology and by its tropism and in vitro cytopathic effect on CD4 (T4) positive cell lines and lymphocytes, but differs from it by lack of hybridization of the genomes and absence of antigenical cross-reactivity of the envelope glycoproteins.

The complete proviral DNA from one HIV-2 isolate (ROD) was cloned, and used to confirm the distant relationship of HIV-1 and 2, this latter being more closely related to a simian retrovirus termed STLV-3 or SIV. Polymorphism is observed by restriction mapping of HIV-2 isolates.

We have sequenced the complete HIV-2_{ROD} genome and observed an overall genetic organization similar to HIV-1. However, the HIV-2 genome is longer (9.6 kb. against 9.2 kb.), mainly because of large insertions in the LTR. The proteins of HIV-1 and 2 are highly divergent, the degree of conservation ranging from 50 % (for gag and pol) to less than 30 % of the aminoacids for the large env glycoprotein, F and Q proteins. Homologous domains in env will be very useful to delineate domains involved in functions common to HIV-1 and 2, such as cell fusion and T4 binding.

TH.1.2 Human and Simian T Lymphotropic Retroviruses: Serologic Identification and Vaccine Development.

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Retroviruses related to HIV have been detected in subhuman primates where up to half of the wild-caught African green monkeys have serologic evidence of exposure to such viruses, designated STLV-3. Following natural exposure monkeys rarely, if ever, develop disease. Using seroepidemiological approaches, healthy people in West Africa were found to be exposed to viruses that are closely related to STLV-3, and designated HTLV-4, LAV-2, HIV-2, SBL-6669, or West African retroviruses (WAR). In some instances such viruses are found in individuals with AIDS-like illnesses. However, seroepidemiological studies did not reveal an association between antibody positivity and disease development.

Infection rates vary widely for different geographical locations in West Africa, but Central Africa seems free from exposure to this virus. HTLV-4 type viruses are transmitted primarily by sexual contact as illustrated by elevated infection rates in female prostitutes. Yet infected prostitutes generally remain healthy and free of lymphadenopathy. Understanding why infection with STLV-3 or HTLV-4 does not pose a high risk for AIDS should be important to determine how to generate immunity in people exposed to HIV.

TH.2.2 Conservation of genome organization between HIV and STLV-3

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Type 3 Simian T-lymphotropic virus (STLV-3) shares many biologic characteristics with HIV, utilization of the T4 molecule as a receptor, syncytia formation in T4-lymphocytes in vitro, similar ultrastructural morphology, Mg+2 dependent reverse transcriptase, major gag-, env-, pol-, and 3'orf-encoded viral proteins of similar size and immunologic cross-reactivity. STLV-3 from African Green monkeys was recently molecularly cloned by virtue of weak nucleic acid cross-reactivity with HIV. Nucleic acid sequence analysis of the 3' 4.2 kb of STLV-3 reveals that HIV and STLV-3 share a similar genome structure. Predicted amino acid sequences of the envelope gene of STLV-3 and HIV share up to 50-55% homology in regions identified as constant domains of the HIV env gene, and analogous positioning of all of 18 cysteine residues in HIV. This indicates that these divergent proteins likely possess a similar backbone structure. Coding regions previously found to be unique to HIV and shown to encode regulatory functions (tat and art) are preserved in STLV-3, indicating that HIV and STLV-3 likely utilize similar regulatory mechanisms (see Viglianti et al). A high degree of conservation of predicted protein sequence was also noted within the 3'-orf region, whose function is unknown, and in the "R" open reading frame for which no protein has yet been identified. This strongly suggests that both genes play an important role in the life cycle of each virus.

TH.1.3 HIV infection in the central nervous system

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The central nervous system (CNS) effects of human immunodeficiency virus (HIV) has recently been acknowledged. CNS involvement may be monitored using psychological testing, computer tomography and magnetic resonance (MR) imaging technique. By combining the MR unit with an imaging enhancing technique reconstruction of different brain regions can be made and treatment effects may be followed by measuring the relaxation times T 1 and T 2.

New treatments using short peptides such as the octapeptide, peptide T are of interest since clinical testing indicate that it appears non-toxic and may have potential benefit. The working hypothesis is that peptide T, D-Ala-Ser-Thr-Thr-Thr-Asn-Tyr-Thr, inhibits HIV-infection by blocking the binding of the viral envelope to the CD4-receptor. Peptide T is a segment of the envelope glycoprotein (gp-12D) of the HIV.

Neuropathological findings in the brains of patients with AIDS are common and suggest that HIV might induce irreversible damage. There is however a discrepancy between the degree of cerebral atrophy and the severity of the CNS symptoms. The new results using reconstructed MR images in patients treated with peptide T suggest that the CNS involvement is at least partly reversible. The methods to test neuropsychiatric dysfunction caused by HIV will be summarized as well as objective measures to follow the presence of HIV in the cerebrospinal fluid.

By mimicking the action of peptides, viral proteins could exert hormonal effects throughout the body, including the CNS, and thus may have a role in the etiology of the progressive dementia of patients with AIDS.

TH.2.3 Molecular characterization of HTLV-4

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A novel human retrovirus, termed HTLV-4, has recently been isolated from West African individuals at high risk for sexually transmissible diseases. This newly discovered virus is related to HTLV-3/LAV in its tropism for OKT4 lymphocytes, the antigenicity of its core proteins, and its in vitro growth characteristics but is clearly distinct from the AIDS virus in its ultrastructure, the size and antigenicity of its envelope proteins, and its apparent clinical sequelae. The existence of these two viruses -- both tropic for OKT4-positive cells yet possessing major differences in protein structure and biologic activity -- provides a unique opportunity to study the molecular biology and structure-function relationships of both HTLV-3/LAV and HTLV-4. We have molecularly cloned the full-length provirus along with unique flanking cellular sequences from two isolates of HTLV-4 and have prepared subclones for transfection and for nucleotide sequence analysis. Comparisons between HTLV-4 and HTLV-III/LAV reveal underlying similarties in gene organization (env, 3'orf, and LTR) although overall nucleotide sequence homology is in the range of only 40%. Interestingly, a peptide sequence from the 3' terminus of the HTLV-III/LAV envelope implicated in its cytopathicity is conserved (12 out of 14 amino acids) in HTLV-4. Structure-function relationships especially concerning the envelope glycoprotein between HTLV-4 and HTLV-III/LAV will be discussed.

TH.2.4 Molecular Cloning and DNA Sequencing Analysis of LAV-2 (Lymphadenopathy Associated Virus Type 2)

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A new subgroup of primate retroviruses serologically related to the human AIDS agent, HTLV-III(HIV) has been recently identified. This includes the simian T-lymphotropic virus type III (STLV-III), isolated from African green monkeys, and three human retroviruses, HTLV-IV, LAV-2, SBL6669, from patients of West African origin. These viral agents share similar morphology, recognize the same receptor, (OKT-4) but show different pathogenetic potential. In vitro all but HTLV-IV are able to kill their target cells. In vivo, in their natural hosts, only LAV-2 and SBL6669 appear to be associated with an immunodeficiency syndrome. In order to better define the genetic relationship between this new subgroup of pathogenic viruses and the HTLV-III(HIV) subgroup and to gain insights into their cytopathic mechanism, we have undertaken the cloning and sequencing analysis of an LAV-2 isolate. The virus was isolated from an AIDS patient originally from Senegal seropositive for LAV-2 antibodies. A permissive cell line, H9, was infected with the viral isolate. The genomic DNA was extracted, partially digested with the restriction enzyme MboI and used to construct a lambda phage library. The library was screened using a cDNA probe homologous to the 3' LTR region of LAV-2 genome. Ten positive clones were detected and characterized by restriction mapping. The results show an overall divergence in restriction sites in comparison to HTLV-III(HIV) restriction map. To further investigate the structure of the LAV-2 genome, we have sequenced the entire genome of the integrated form of LAV-2 using the Sanger dideoxy technique. The results of this analysis will be presented.

TH.2.5 Characterization of a Pathogenic Lentivirus From Cattle Which is Structurally, Immunologically, and Genetically Related to the Human Immunodeficiency Virus (HIV)

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An infectious retrovirus was previously isolated from leukocytes of a cow with persistent lymphocytosis, lymphadenopathy, CNS lesions, progressive weakness, and emaciation (Van Der Maaten et al., J. Natl. Cancer Inst. 49:1649, 1972). *In vitro* the virus replicates and induces syncytia in cells derived from various embryonic bovine tissues, including brain. By electron microscopy, the virus morphologically resembles HIV and other pathogenic lentiviruses. This virus, designated BIV (bovine immunodeficiency-like virus), possesses a major protein band of 26 kD (p26) and several smaller and larger virus-specific protein bands by SDS-PAGE. A rabbit antiserum to BIV reacts strongly in immunofluorescence assays to HIV-infected cells and on Western blots with p26 and p24, the major core proteins of BIV and HIV, respectively, but not those of visna or caprine arthritis encephalitis viruses. A competitive radioimmunoassay using the rabbit anti-BIV serum and ^{125}I-labeled HIV p24 was developed. Consistent with the Western blotting data, disrupted BIV and STLV-III competed equally well with HIV p24 in this assay, whereas other lentiviruses competed poorly or not at all. Molecular clones of BIV proviruses have been isolated from a λ library constructed from genomic DNA of BIV-infected cells using a cDNA probe made from BIV viral RNA. These clones hybridize with *pol* gene probes made from HIV and visna virus. DNA sequence analysis of the 5' *pol* gene region of BIV has enabled us to construct a phylogenetic tree elucidating the relationship of BIV to other lentiviruses.

TH.2.6 Immune Selection of Antigenic Variants of Equine Infectious Anemia Virus May Occur Through Elimination of Infected Cells Rather Than Through Neutralization of Cell Free Virions

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The morphological, genetic, and serological relatedness between equine infectious anemic virus (EIAV) and human immunodeficiency virus (HIV) has increased interest in understanding the role of variation of EIAV in viral persistence and the host response to infection. EIAV was isolated from peripheral blood leukocytes collected during two, early, febrile periods of an experimentally infected horse. These isolates, referred to as MA-1 and MA-4, were shown to be genetic and antigenic variants by RNase T_1-resistant oligonucleotide fingerprint analyses and membrane immunofluorescence of infected cells. The finding that variant-specific epitopes of EIAV were expressed on the surface of infected cells indicated that immune selection of viral variants might occur through immunologically-mediated destruction of EIAV-infected cells. Furthermore, antibody to variant-specific cell surface antigens was detectable prior to the development of virus neutralizing antibody. This suggested that neutralization of cell-free virions may not be important in the selection of EIAV variants.

Biochemical identification of viral proteins expressing variant-specific antigens was assayed by radioimmunoprecipitation (RIP) using detergent lysates of EIAV-infected cells. Early immune serum, specific for MA-1 by membrane immunofluorescence, was found to be broadly reactive by RIP. This apparent paradox indicated that EIA viral antigens exposed in detergent lysates were highly cross-reactive, whereas viral antigens exposed on the surface of live cells were strain-specific. These data caution against the use of immunoassays which rely on detergent treatment of antigens in looking for strain-specific antibody with potential biological importance in variant selection.

Health Care—Patient Care, Attitudes, Knowledge, and Risks

TH.3.1 Helping Young People Face Death: Resuscitation Status and Outcome in First Episode Pneumocystis Carinii Pneumonia (PCP)

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Since the onset of the AIDS epidemic in 1981, ICU use for a group of patients with a uniformly fatal disease has been frequently questioned. Addressing this issue, all first episode PCP admissions at San Francisco General Hospital were reviewed for the last six months of 1986 (N=115), and DNR choice, ICU use, and outcome (death or discharge) were noted.

DNR Status	No. Patients	ICU Admit	Discharge or Death	
Full code	10	0	10	0
DNR	55	0	42	13
Code, then DNR	4	4	1	3
Code status not addressed	46	0	46	0

This pattern of ICU use reflects the added knowledge on the part of the house staff, attending physicians, and patients of the poor prognosis of patients with AIDS requiring ICU admission. With this knowledge, less than 10% of patients chose to be on full code status.

Patients should be given the early opportunity to discuss their resuscitation status, and counseled regarding the poor prognosis for PCP patients who require intubation. A multidisciplinary approach to the patient's choice, using medical, nursing, and counseling resources, allows the patient and family to best understand the implications of their decision. This decision will become more complex as potentially effective antiretroviral therapy for AIDS becomes available. Therefore, we will be monitoring patterns of choice during January -June 1987.

TH.3.2 Housestaff Attitudes Towards The Acquired Immunodeficiency Syndrome.

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Care of AIDS patients elicits strong emotional and psychological responses in providers. In September 1983, we surveyed medical houseofficers (HO) at UCSF, addressing estimation of risk to health care workers (HCW's), anxiety elicited in HO's and satisfaction in the care of AIDS patients. 68% of respondents felt HCW's were at risk of acquiring AIDS. Men and women HO's differed significantly in their estimation of risk: 84% of men versus 48% of women agreed HCW's were at risk (p=0.004). Sense of risk affected precautions followed with significantly more men reporting mask use and glove wearing. >80% of medical housestaff were at least mildly anxious about taking care of AIDS patients and estimated that 20% were "very anxious". 97% reported worrying about getting AIDS at least on occasion. 35% reported worrying about giving AIDS to a family member, 20% reported dreams or nightmares about AIDS and 18% reported symptoms which they felt were suspicious of AIDS. Men were more likely to report their preoccupation, dreams and nightmares and rated their anxiety significantly higher than did the women respondents (p=0.03). Housestaff chose the midpoint of a 4 point Likert scale when asked to express satisfaction. Increased contact with AIDS patients predicted a less negative response with 68% of HO's who had cared for <10 patients disliking AIDS care compared to 35% who had cared for >10 (p=0.02). To a large extent these responses are gender dependent. HO's have responded to this lethal epidemic with expertise and compassion but need more assistance in handling the stress induced by assuming their professional responsibility.

TH.3.3 Concerns of Medical and Pediatric House Officers about Acquiring AIDS from their Patients

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To assess the degree of house officers' concerns about acquiring AIDS from their patients, we surveyed medical and pediatric residents in four New York residency programs with large AIDS patient populations. During the study period, 2/1/86-5/1/86, multiple choice questionnaires were distributed to all house officers present at the study sites (outpatient clinics) and were completed anonymously. Of 263 questionnaires distributed, 258 (98%) were returned. Thirty-six percent of medical and 17% of pediatric house officers reported needlestick exposures to blood of AIDS patients. Forty-eight percent of medical and 30% of pediatric house officers reported a moderate to major concern about acquiring AIDS from their patients. Thirty percent of all respondents believed concern about AIDS increased the stress of their residency moderately to extremely.

Multivariate analysis demonstrated that a greater concern about personal risk was independently associated with an increased number of AIDS patients treated (p=0.01), the year of residency training (greater concern in earlier years, p=0.002), and the type of residency program (greater concern in medical than pediatric house officers, p=0.0003). A history of needlestick exposure was not significantly associated with increased concern (p=0.4). Thirty percent of all respondents indicated they would want to know their current HIV serology status. Ninety-three percent of respondents believed concern about acquiring AIDS did not adversely affect their care of patients; however, 25% stated that they would not continue to care for AIDS patients if given a choice. The results demonstrate a considerable degree of concern about acquiring AIDS among house officers caring for AIDS patients and suggest the need for housestaff training programs to formally address these concerns.

Clinical Studies—Opportunistic Infections

TH.3.4 AIDS Train the Trainer Program for Health Care Providers: California Nurses Association's Innovative Approach

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Many health care providers still harbor fears and misunderstandings about AIDS that negatively affect the delivery of patient care. In order to resolve these fears and misunderstandings, the California Nurses Association, working with the AIDS Project Los Angeles and the San Francisco AIDS Foundation, developed, implemented, and evaluated an innovative AIDS "train the trainer" program. The program was designed to replace didactic lectures with more effective methods to meet the needs of adult learners. By April 1987, 27 two-day trainings were conducted throughout California to certify 750 key health care providers in both adult learning principles and AIDS content. Creative teaching strategies such as guided fantasy, role play, and simulation were utilized to encourage group interaction and the analysis of sensitive issues underlying the fear of AIDS. By May 1, the 750 certified AIDS educators had each conducted instructional programs for groups of 25 or more health care providers, including direct care providers, support services personnel, and administrators. A total of 18,750 people were educated in these secondary trainings. Summative evaluation of the primary trainings indicates that this model is effective for increasing trainers' competence and confidence related to teaching about AIDS and HIV infection. Summative evaluation of the secondary trainings is still in process.

TH.3.5 Low Occupational Risk of HIV Infection for Dental Professionals (DP).

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In Oct. 1985 we began a study of the prevalence of serum antibodies (Abs) to HIV in DP recruited via a mailing and at professional meetings. Subjects completed questionnaires on demographics, type, duration and location of practice, AIDS high risk behavior, precautions used in treating patients (pts), and types of pts treated. HIV Abs were assayed by EIA, with Western blot confirmation of positives. Homosexual men and parenteral drug abusers were excluded.

Of 1009 subjects, 919(91%) were dentists, 90 hygienists; 807(80%) were male. Major types of dental practice were restorative(52%) and oral surgery(5%). 324 DPs(32%) practiced in the New York City area, 43(4%) in Miami, and 20(2%) in Houston, Los Angeles, or San Francisco. 116/988 respondents(12%) had treated known AIDS pts (median 2,range 1-78), 708/983(72%) members of AIDS risk groups. At time of screening 313/977(32%) used gloves at all times, 579(59%) for selected pts or procedures, 85(9%) never. Eye protection was used by 581/899(65%) always, 238(27%) sometimes, 80(9%) never. 531/936(57%) had increased use of precautions since 1983, 83% at least partly due to concerns about AIDS. 895/987 (91%) reported accidental parenteral puncture wounds by instruments; median number per subject over the preceeding 5 years was 10(range 1-1000). 568/1002 respondents (57%) had not received hepatitis B vaccine; of these, 122/546 tested (22%) had Abs to hepatitis B surface antigen.

None of the 1009 subjects had Abs to HIV confirmed by Western blot.

Therefore, DP appear to be at very low risk of occupational acquisition of HIV infection (95% C.I., 0 to .003), even though recommended precautions are not always used and accidental parenteral puncture wounds are frequent. Routine use of recommended precautions should make any risk even more remote.

TH.3.6 Prevalence of Unsuspected Human Immunodeficiency Virus In Critically Ill Emergency Patients

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Implementation of recommended guidelines for prevention of transmission of the human immunodeficiency virus (HIV) to health care workers is not uniform, and in part is based on a lack of recognition of the extent of asymptomatic HIV infection in this country. In order to reinforce the need for appropriate infectious disease precautions, we tested for HIV antibody seropositivity in 203 critically ill patients presenting to an urban emergency department, none of whom had a previous diagnosis of HIV infection.

We found that 6 (3%) of the total were seropositive by both enzyme-linked immunoassay (ELISA) and Western Blot, and that these 6 represented 16% of the 37 patients between 25 and 34 years of age. All seropositive patients were victims of trauma, and of 10 gunshot wound victims between the ages of 25 and 34, 3 (30%) were seropositive.

None of the seropositive patients had been suspected of being infected, all were actively bleeding, and all required multiple invasive procedures, including by paramedics in the field and by physician staff in the emergency department.

These results reinforce the necessity of infection control precautions, whether or not previous suspicion of HIV infection exists.

TH.4.1 Preliminary Results of a Phase I-II Trial of Trimetrexate Therapy for Pneumocystis Pneumonia in AIDS Patients

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Trimetrexate (TMTX), a potent inhibitor of dihydrofolate reductase, has been shown in laboratory studies to have potential advantage over conventional agents for therapy of Pneumocystis carinii pneumonia (PCP). In this trial, AIDS patients with histologically proven PCP (first or subsequent episode) were treated with TMTX (30 mg/M^2 QD x21 days) plus leucovorin (LVN) (20 mg/M^2 Q6h x 23 days) ± Sulfadiazine (S) (1.0 g Q6h x 21 days). Pharmacokinetics of TMTX were highly predictable with a t 1/2 of 9 hours. Toxicity possibly related to TMTX was minimal, consisting of purpuric rash (1/42 patients), mild granulocytopenia (5/42 patients) and thrombocytopenia (8/42 patients), plus mild transaminasemia (8/42 patients). Cytopenias were easily managed by dose adjustments of TMTX or LVN. Complete responses were seen in 9/13 previously untreated patients who received S + TMTX/LVN; 9/14 previously untreated patients who received TMTX/LVN without S; 9/13 patients who failed conventional therapy and received TMTX/LVN without S. Relapses within 1 month were seen in 5 patients. Results of this trial indicate that TMTX ± S is an effective and well tolerated therapy for PCP, the relative merits of which need to be compared to conventional agents in a larger controlled trial.

TH.4.2 Studies on Successful Eflornithine Treatment of Pneumocystis Carinii Pneumonia (PCP) in AIDS Patients Failing Conventional Therapy

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Eflornithine (E; DL-α-difluoromethylornithine) is an irreversible inhibitor of ornithine decarboxylase with activity against several protozoan species related to Pneumocystis carinii (PC). This antiprotozoan activity, plus dramatic therapeutic results in a few patients, led to compassionate E use by 189 investigators treating 345 AIDS patients with proven PCP. The patients, entered because of treatment failure and/or intolerance to trimethoprim-sulfamethoxazole (TMP-SMX) and/or pentamidine (P), had no therapeutic alternatives and little or no chance for survival. The recommended E dose was 100 mg/kg I.V. q6h for 14 days followed by 4-6 weeks oral therapy at 75 mg/kg q6h. Efficacy was measured by survival to hospital discharge and clinical response evaluated from changes in arterial blood gases, chest X-ray, defervescence and followup lung biopsy. Survival for patients receiving >4 days of E therapy (266/345) was 10/101 (10%) in patients receiving mechanical ventilation (MV) at study entry and 109/165 (66%) for spontaneously breathing (SB) patients at study entry. Survival for subjects receiving ≥14 days E treatment (160/345) was 10/43 (23%) for MV patients and 91/117 (78%) for SB patients. Clinical responses were higher: 27/43 (63%) MV patients completing ≥14 days therapy and 102/117 (87%) SB patients had positive responses. Followup examinations showed clearing of PC in 30/74 (40%) patients; the relationship between the disappearance of the cysts and survival was significant ($p < .05$). E was generally well tolerated with thrombocytopenia (48%), diarrhea (20%) and leukopenia (16%) reported as the most frequent adverse events. The survival, clinical response and clearing of PC in patients with little/no expected survival demonstrate E effectiveness comparable to first line treatment with TMP/SMX and P.

TH.4.3 Cyclosporin A may induce deterioration in patients with AIDS.

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The pathogenesis of AIDS remains unclear but it may be in part an immune-cytopenia. The lack of efficacy of other therapies and the proven benefit of Cyclosporin A (CyA) for many patients with immune cytopenias as well as favourable reports from French investigators prompted this study in the belief that CyA might ameliorate some of the immunoregulatory disturbances involved in AIDS.

Eight stable AIDS patients were treated for a mean duration of 49 days with biologically active doses of CyA. Clinical, hematologic, immunologic, renal and hepatic functions were followed at least weekly before, during and after administering CyA.

The white count, lymphocyte count, hemoglobin, platelet count, total T cells, T4 and T8 cells fell significantly during treatment. HIV-1 was cultured more frequently during treatment. The white blood count, platelet count, total T cells and T8 cells reached pre-treatment values after therapy was withdrawn. Hemoglobin remained significantly lower than prior to treatment and T4 cells rose towards pre-treatment values but did not reach statistically significant levels.

Severe toxic symptoms, not characteristic of CyA therapy in other patients, affecting functional capacity were experienced by all 8 patients and necessitated discontinuation of the drug in 6. The symptoms included nausea, vomiting, anorexia, fatigue, pain and extreme swelling and increased number and size of Kaposi's lesions.

CyA does not improve, and may worsen the symptoms and laboratory findings in AIDS.

TH.4.4 Cytomegalovirus and Adenovirus Infections: Response to DHPG.

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Infections with human cytomegalovirus (CMV) show marked sensitivity to treatment with DHPG in vitro and this drug has proven clinical efficacy against disease in AIDS patients. We now have evidence that infections with adenoviruses also respond to treatment with DHPG, which maybe important in the clinical management of opportunist infections in AIDS patients. Patients suffering pneumonitis, retinitis or colitis were treated with DHPG on the basis of virological, histological or clinical evidence that CMV was the aetiological agent. During these investigations, repeated isolations of CMV and/or adenovirus was made and viruses were characterized by restriction analysis of viral DNA after comparison with prototype strains. Plaque-reduction assay showed the sensitivity of adenovirus isolates (ED50 7 to 10 μM) to DHPG was about 10-fold lower than values recorded for CMV, but within the range of concentrations achieved during treatment (peak levels 46 - 56 μM 15 minutes post-infusion 500 mg/kg bd). Sensitivity of adenovirus isolates in cell culture was confirmed by studies using high multiplicity of infections. The clinical, virological and molecular aspects of the study will be illustrated by comparison of three AIDS patients all treated with DHPG from whom 1) only CMV, 2) only adenoviruses, 3) both viruses were isolated.

TH.4.5 Successful Therapy of Cytomegalovirus (CMV) Infections in Patients (pts) with Acquired Immunodeficiency Syndrome (AIDS) with Ganciclovir (DHPG)

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Since January 1985, 122 pts with AIDS and severe CMV infection were treated with DHPG. 118 were male, 4 were female. 117 males were homosexual, 1 male and 1 female had transfusion related AIDS, 3 females were sex partners of IV drug users. The mean age was 38 years. 25 had Kaposi's sarcoma, 70 had PCP and 36 had both. Diagnosis of CMV was made on positive tissue biopsy, a positive urine culture or positive fundoscopic exam. Responses were measured clinically and virologically by objective criteria including endoscopy. Sites of CMV were: colon and rectum 51 (42%), retina and CNS 46 (38%), esophagus, stomach and small bowel 14 (11.5%), lung 9 (7%) and liver 2 (1.5%). DHPG was administered at a dose of 5 mg/kg IV BID for 14 days. On relapse pts were retreated and placed on maintenance (M) of 6 mg/kg daily. Clinically, 88 of the 122 improved (72%), 8 stabilized (6.5%) and 22 worsened (18%), 4 were not evaluable (3.2%). 107 pts survived for more than 4 weeks. Overall median probability of survival was 19 weeks with a median follow up of 16.6 weeks. 59 (48%) pts became culture negative, 16 (13%) did not change. 47 (39%) were not evaluable. Reversible leukopenia < 2,000 occurred in 6/122 and skin rashes in 4/122. 62 pts received M with DHPG. Probability of survival of pts on M was 33 wks compared to 18 wks on no M $p < 0.001$. In PCP pts, probability of survival from date of PCP was 45 wks on M, compared to 35 wks for pts not on M $p < 0.001$ (controlled for PCP prophylaxis). We conclude that Ganciclovir (DHPG) is effective in the treatment of CMV in AIDS pts. A high proportion of pts will relapse, M treatment may be associated with an increased probability of survival.

TH.4.6 A Clinical Trial of Recombinant Alpha Interferon in Patients with AIDS

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We report the results of a randomized, double-blind, placebo-controlled trial of recombinant interferon-alpha-2A (Roferon®-A) in unselected AIDS patients without Kaposi's sarcoma. Sixty-seven patients were enrolled and received 1 of 3 regimens: placebo or 3 or 36 million units of Roferon®-A 3 times weekly IM for 12 weeks. The 3 groups were comparable in number of patients, age, gender, risk behavior, clinical measures of HIV infection, and initial T4/T8 ratios. Thirteen patients received less than 4 weeks of therapy, 54 patients were thereby available for efficacy analysis.

There were no significant differences in survival or rate of opportunistic infection during or after treatment in the 3 groups. A significant decrease in T8 cells occurred in the 3 million unit group but no significant differences in T4, total lymphocytes or T4/T8 ratio occurred. There were no significant differences in adverse drug reactions including those in central nervous and GI systems, or laboratory findings among the 3 groups. Six patients required reduction in dose because of side effects, 4 in the 3 million and 2 in the 36 million group. Seven patients dropped out due to adverse reactions, 2 in the 3 million group, 4 in the 36 million group, and 1 in the placebo. The preliminary analysis of this study did not demonstrate effectiveness of Roferon®-A in the treatment of unselected AIDS patients without Kaposi's sarcoma. However, the drug was acceptably tolerated and might have a role in therapy of AIDS patients in combination with other agents.

Prevention/Public Health—Drug Users and Other High Risk Groups

TH.5.1 High Rate of HTLV-III/HIV Exposure in IVDA's from a Small-Sized City and the Failure of Specialized Methadone Maintenance to Prevent Further Drug Use

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To investigate the seroprevalence to HTLV-III/HIV and HTLV-I in a non-metropolitan area in New England, we conducted a voluntary screening program in New Bedford, MA, from April 1986 to December 1986 at the only drug treatment center serving this predominantly Caucasian community of 100,000. Of greater than 300 clients, 114 chose to be screened in our program. 27 clients (24%) were found to be seropositive for HTLV-III/HIV and none were found to be seropositive for HTLV-I.

All seropositive clients were given individual, long-term counseling and medical follow-up in addition to the opportunity to receive "methadone maintenance", instead of simply short-term drug detoxification with methadone. Positions in the otherwise full methadone maintenance program were still offered to all seropositive clients. Even with additional counseling, medical care, and priority for entrance and continuation on methadone maintenance, 67% (18/27) returned to I.V. drug use as determined by urine drug screens, personal histories and drop-out rates in the 6 months since initiating this specialized methadone maintenance program. This is compared to 7% (10/134) for the entire established methadone maintenance program over the same period, and to 24% (6/25) for a group of seronegative clients, and to 8% (2/25) for a group of "never tested" clients who were matched by age, sex, employment status, and drug usage at the beginning of the 6 month folow-up of the seropositive cohort.

The high rate of seropositivity to HTLV-III/HIV in this smaller sized community and the lack of compliance to a novel attempt at curbing continued I.V. drug use among seropositivies makes the call for new programs geared to prevention of viral transmission in this population all the more urgent and difficult.

TH.5.2 A Coupon Program: AIDS Education and Drug Treatment

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In New Jersey, IV addicts comprise the majority of AIDS cases, but under 10% are currently enrolled in a drug treatment modality. Imposition of patient fees in 1981 resulted in a loss particularly of black males. This paper describes an effort by the NJSDH beginning in September 1986 to induce addicts into treatment and to provide AIDS education to reduce the rate of HIV transmission.

Serially numbered coupons, redeemable for a free outpatient detoxification, were distributed in inner-city neighborhoods by previously established ex-addict AIDS outreach workers. Eligible recipients were IV drug abusers who had not sought treatment in at least one year. Programs were reimbursed under contract for collecting demographic data on coupon bearers, providing heroin detoxification and priority for extended treatment, providing one hour of AIDS education with pre- and post-testing, and maintaining a file matching coupon numbers with patient names.

By January 15, 1987, of 607 coupons distributed, 76% had already been redeemed. Coupon redeemers were 76% black and 81% male. Fifty-four percent had ages between 26 and 35 and 40% were over 35; 41% had no previous treatment attempts and 44% had 1-3 attempts. AIDS education had been provided and pre- and post-tests administered to over 90% of redeemers. The program appears successful in meeting its goals.

TH.5.3 Evidence of Reduced AIDS-associated Risk Behavior in Homosexual/Bisexual Men but Not in Heterosexuals or IV Drug Users in 4 Widely Dispersed U.S. Counties.

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Since hepatitis B virus and human immunodeficiency virus have remarkably similar transfusion patterns, epidemiologic changes in one should mirror epidemiologic changes in the other. We have used changing epidemiologic patterns of hepatitis B in 4 U.S. counties, 1 each in Florida, Alabama, Colorado and Washington as an indicator of the effectiveness of AIDS prevention measures (presumably individual behavior changes). In these 4 counties there was, for the first time, a dramatic change in hepatitis B cases associated with homosexual behavior (20% of all cases in 1985 versus 9% in 1986). In contrast there was a relative and absolute increase in the number of IV drug-related cases (16% vs. 27%) and documented heterosexual-intercourse-related cases (12% vs. 18%). Racially there was little change (approximately 2/3 white and 1/4 black) but there was a 10% increase in female cases (33% in 1985, 43% in 1986).

From these data it can be inferred that the AIDS-prevention message has been heard and acted upon by a considerable number of homosexually active men across the United States, but similar behavior change is not yet apparent among either heterosexual men and women or IV drug users.

TH.5.4 Use of Condoms for the Control of AIDS: A Cross-Section Study in Rikai District, Uganda.

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AIDS, locally known as "SLIM" has been known in Uganda since late 1982, and then described as an obscure wasting disease. It was not until late 1984 that the disease became associated with AIDS, as proven by serologic tests. The areas most greatly affected are Rakai and Masaka Districts. The incidence rate in Rakai was 0.12% in 1986. Amongst preventive measures instituted was the distribution of condoms primed by a health education campaign. By August 1985, 20,000 were distributed.

Recommendations of the Regional Conference on AIDS in Africa (Brazzaville: November 1986) include studies of attitudes on condom usage and methods to increase availability, distribution and use of condoms. A study has been initiated in the Rakai District to determine attitudes and use of condums among randomly-selected cohort of sexually-active adults. Market places are good venues for cross-sectional selection in rural Uganda and comprise the study sites. Mature, experienced health professionals administer standardized interview forms and record responses to questions regarding subject's biodata, knowledge and use of condoms, and knowledge and affect on sexual behavior of AIDS. Interview records are serially numbered and names deleted to ensure confidentiality. Data will be analyzed categorically, subjected to significance test, and presented in tables and graphs.

TH.5.5 Effect of an AIDS education program on increasing condom use in a cohort of Nairobi prostitutes

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In order to control sexual transmission of HIV, modification of sexual behaviour through education must be achieved. We have been studying cohort of Nairobi prostitutes for 24 months who are at high risk of HIV infection (over 80 % positive) and pose a substantial risk to their clients. Beginning in November 1985 we provided education on AIDS to this cohort of 596 women. Several different methods of education - public meetings, individual counselling on the basis of HIV results and general health education - were employed. In June 1986 distribution of condoms through the clinic began. In October 1986 we began surveying the frequency of condom use in the cohort. 126 women who were newly recruited served as controls. Some condom use was reported by 8 % of women prior to the education program vs. 90 % of the most intensively educated group (Grp I), 85 % of the less intensively educated group (Grp II) and 73 % of the control gropu (Grp III). In Grp I and II no condom use was reported by 5/61 women who received counselling vs 10/33 women who did not receive counselling ($p < .05$). HIV antibody status did not influence frequency of condom use. Condom use was more frequently client initiated in the control group. We have witnessed a remarkable increase in condom use as a result of the program. Although more intensive education resulted in incremental increases in condom use, minimal education with provision of condoms was the most important step.

TH.5.6 Drug Use and Sexual Behavior Change in a Cohort of Homosexual Men

DAVID G. OSTROW, M. VAN RADEN, L. KINGSLEY, R. FOX, J. DUDLEY, R.A. KASLOW, and the Multicenter AIDS Cohort Study (MACS).

We have examined the association between the use of recreational drugs (marijuana, cocaine, volatile nitrites, amphetamines, sedatives, hallucinogens and opiates) and sexual behavior in a cohort of 5,000 homosexual/bisexual men residing in Chicago, Baltimore/Washington, D.C., Los Angeles and Pittsburgh. At both baseline and six month follow-up evaluations, men using recreational drugs were significantly more likely to be engaging in sexual practices believed capable of transmitting HIV infection. These associations were strongest when drug use with sexual activity was examined and were independent of the number of sexual partners. Furthermore, when changes in sexual behavior were examined, men who had been using recreational drugs were significantly less likely to have reduced their level of unsafe sexual behavior than men not using drugs (relative risks ranging from 1.2 to 2.2 for each drug examined). These findings provide a possible explanation for the observation of a higher prevalence of HIV antibody positivity in MACS participants using recreational drugs and suggest intervention strategies for controlling the sexual spread of HIV infection.

Roundtable Discussion

TH.6 Developing Community Based Service Organizations

Panel Organized By: Paul Kawata
National AIDS Network
Washington, D.C.

Tim Wolfred, San Francisco AIDS Foundation, San Francisco, California

Richard Dunne, Gay Men's Health Crisis, New York, New York

Judith Peabody, Gay Men's Health Crisis, New York, New York

Epidemiology—Perinatal Transmission and AIDS

TH.7.1 National Trends in Perinatally Acquired AIDS, United States.

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As of January 19, 1987, 423 children under 13 years of age with AIDS have been reported to CDC; the number of cases is currently doubling every 13 months. Perinatally acquired cases (PA) continue to predominate, accounting for 338 (80%) of cases; 24 (6%) are hemophiliacs, 50 (12%) are children infected through transfused blood, and 11 (3%) have incomplete risk histories; no case acquired through household, school or daycare contact has been reported. Notably, the geographic distribution of children with PA is changing. The proportion of cases outside the high-risk areas of New York, New Jersey and Florida has increased from 21% of cases diagnosed through 1984 to 37% of cases diagnosed in 1985-1986 ($p=0.002$). This trend is consistent with the trend among women with AIDS, which shows an increase from 23% to 32% in cases reported outside these high-risk areas. The risk factors of mothers of children with PA are also changing; the proportion of mothers infected through heterosexual contact has increased from 34% of PA cases diagnosed through 1984 to 44% of cases diagnosed in 1985-1986 ($p=0.01$); nearly all other mothers are IV drug abusers. PA continues to affect mostly blacks (64% of cases) and Hispanics (25%), with cumulative incidences in these respective populations 29 and 18 times the rate among whites. Although older children with AIDS are being increasingly recognized, the median age at diagnosis has remained constant at 6 months, reflecting increasing seroprevalence rates in childbearing women. Compared to children older than 1 year of age when diagnosed, children diagnosed under 1 year of age are more likely to have Pneumocystis carinii pneumonia as an initial opportunistic infection (71% vs 36%), and have a poorer prognosis (median survival time after diagnosis of 4 months vs 22 months).

TH.7.2 Perinatal Transmision of HIV in Intravenous Drug Abusers (IVDAs)

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To determine the rate and outcome of perinatal transmission of HIV to infants we are prospectively studying pregnant IVDAs and their offspring. Women in a NYC methadone program (MMTP) receive prenatal care and HIV serum antibody (Ab) testing. Infants are examined at birth and at 3 month intervals, and monitored for growth and development and signs of illness. Cord and peripheral blood are tested serially for HIV Ab and cells stored for HIV culture.

Since 9/85, we have studied 16 infants of 15 seropositive (SP) mothers and 30 infants of 29 seronegatives (SN). Mothers did not differ by age or obstetrical complications. 14/15 (93%) SPs were non-white vs. 18/29 (62%) SNs ($p<.05$). Infants did not differ in frequency of intrapartum fetal distress, APGARs, gestational age, or neonatal complications. Mean birthweight was 2860g for SPs, 2830g for SNs. Of 12 infants of SP mothers tested, all had HIV Ab in cord or neonatal specimens; none of 17 infants of SNs had HIV Ab at birth or thereafter. No infant has AIDS to date. One SN died from sudden infant death syndrome. 12 infants of SP mothers had HIV Ab tests $\geq$ 4 weeks of age (mean of 27 wks. at last follow-up); 6 remain SP (50%), 6 became SN (50%). Those becoming SN had mean age at first negative Ab test of 34 wks. (range 12- 55). 1/6 infants SP at last test was healthy, 5 had either: failure-to-thrive (FTT)(3), developmental delay(3), lymphadenopathy in $>$ 2 sites (LA)(3), persistent oral thrush(1), or multiple bacterial infections(BIs). 5/6 infants becoming SN were well; 1 had FTT, LA and BIs. 2/17 infants of SN mothers (mean age 30 wks.) had LA(1) or BIs(1).

Results show that maternal HIV Ab was not associated with adverse peri-or neonatal infant outcome. Preliminary data showed that 6/12 (50%) of infants of SP mothers became SN within 1 year; 5/6 of these infants remained healthy. The rate of HIV transmission may be $<$60%. 5/6 (83%) infants retaining HIV Ab had possible HIV related disease. Similar clinical findings in 1/6 infants who became SN suggest that HIV Ab testing may be $<$100% sensitive for HIV infection in infants.

TH.7.3 Human Immune Deficiency Virus in Pregnant Women and their Offspring

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The effect of HIV on pregnancy, the rate of perinatal transmission, and a description of perinatally acquired HIV infection are important aspects of the natural history of HIV. We are studying the perinatal transmission of HIV on drug using (DU) and Haitian (H) populations. Pregnant women are identified in the prenatal clinics. Demographic, sexual, drug use, and medical histories are obtained. Evaluations (clinical and laboratory) are performed in the mothers pre- and post-partum and in the infants at regular intervals. As of January 15, 1987, 89 women have been enrolled. Sixty-five infants have been born, 44 to DU mothers and 21 to H mothers [27 (42%) to seropositive (SP) mothers and 38 (58%) to seronegative (SN)]. The SP and SN women from the DU and H cohorts have been compared on the basis of background factors and with regard to obstetrical, perinatal, and post-partum outcome. The infants have been compared with regard to birth weight, gestational age, and perinatal problems. The mean duration of the pediatric follow up is 5.5 months (range 0-12 months). Two infants have AIDS, three have persistent hepatosplenomegaly and lymphadenopathy, and four have persistently palpable lymph nodes in multiple anatomical sites. Data will be presented on the expansion and continued follow up of these groups.

TH.7.4 PROSPECTIVE STUDY ON NEWBORNS OF HIV SEROPOSITIVE WOMEN.

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The exact incidence of materno-foetal transmission of HIV as well as the natural history infection in infants is not yet well known. We have conducted a prospective study on newborn of HIV seropositive mothers in Paris area since september 1985. To date, 158 children are enrolled with a mediam rate of increase of 3 children per week. These children were clinically examined monthly during the first 18 months. The presence of IgG HIV antibody by Western Blot and viral antigen (p25, Abbott Lab) were evaluated at birth, 9 months, 18 months or earlier if symptoms occurred. Immunological investigation were performed simultaneously. HIV infection of infants was proven by persistance of positive IgG HIV antibody after one year of age and/or occurrence of clinical or immunological symptoms. The analysis of the first 34 observations have shown that 14 infants are infected and 20 are free of HIV (infection rate ≃ 40 %). Only one out 158 newborn had HIV-associated clinical manifestation at birth. The mean age of the first symptoms was 6 months ± 2. Normal number of CD4 + and CD8 + T lymphocytes were found at birth except in the symptomatic child. Our preliminary results show that the procedure used for the detection of HIV antigen p25 is not as useful as expected for an early diagnosis of virus infection since only 4/48 cord blood samples were found positive.

TH.7.5 Congenital transmission of HIV in Nairobi, Kenya

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Transmission of HIV from mother to child is a major public health problem. To determine the risk of congenital transmission of HIV, we screened the sera of 2265 women in labour at the Pumwani Maternity Hospital, Nairobi, Kenya for HIV Ab. 62 women were seropositive for HIV Ab by ELISA and WB assays (HIV +). 124 seronegative mothers and their newborns served as a control group. Maternal age, marital status, parity, and prior stillbirths and miscarriages were similar in cases and controls, but HIV + mothers were more likely to have had previous infant deaths (15/90 livebirths vs 15/213, $p < .02$). Infants of HIV+ and HIV- mothers were similarin birthweight, gestational age, and Apgar scores but infants of HIV+ mothers had a higher prevalence of palpable lymph nodes at birth (24/50 vs 22/103, $p < .001$).

Sera from cord blood of infants of HIV+ mothers were analyzed for HIV IgG and IgM Ab. All 53 sera tested were positive for HIV IgG Ab by ELISA and WB and 9/53 (17 %) were positive for IgM Ab by WB. Three correlates of infant IgM Ab were identified; a history of prior infant deaths (7/21 vs 8/67, $p < .03$), incurrent maternal infection during pregnancy (4/6 vs 6/39, $p < .02$) and maternal lymphadenopathy (6/6 vs 23/37, $p < .08$). If HIV IgM Ab in cord blood accurately reflects in utero infection, these results suggest that congenital transmission of HIV occurs in only 17 % of affected pregnancies. Cord blood lymphocyte cultures, serial IgG and IgM Ab assays, and clinical follow up will determine if cord blood IgM Ab is an accurate marker of in utero HIV infection.

TH.7.6 Perinatal HIV Transmission in Two African Hospitals.

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Twenty four hundred of a target population of 7000 women have been enrolled in a longitudinal congenital HIV transmission study; 135 (5.6%) were HIV(+). Age, parity matched, pregnant control women have also been selected. Lymphocyte cell typing, HIV cultures (antenatal maternal and cord blood) and maternal examinations and cultures for other sexually transmitted diseases have been obtained.

Seventeen (45.9%) of 37 infants born to HIV(+) mothers had HIV IgM antibodies (Western blot). Women delivering infected children had a significantly lower mean T-Helper/T-Suppressor ratio (Th/Ts) [ratio of .55] than infected women delivering non-infected infants(Th/Ts=.99), or non-infected control women [Th/Ts=3.53]. The Th/Ts ratio in cord blood of infected infants (Th/Ts=2.7) was no different than the ratio in noninfected infants (Th/Ts=2.3). Three (17%) of 18 placentas of infected women but none of 23 placentas of non-infected women showed unusual perivascular calcifications. Twenty (39%) of 51 HIV(+) mothers reported having lost at least one infant prior to their current pregnancy compared to 9 (16%) of 55 HIV(-) mothers (p=.01).

Congenital transmission of HIV infection is not rare in Africa. A low maternal antenatal Th/Ts ratio is associated with congenital HIV infection. HIV(+) pregnant women in an advanced stage of their disease are more likely to infect their children in utero.

Clinical Management—Infections I

TH.8.1 Treatment of Cytomegalovirus Retinitis with Trisodium Phosphonoformate (Foscarnet)

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Cytomegalovirus (CMV) is a frequent cause of retinitis and a leading cause of blindness in patients with the Acquired Immunodeficiency Syndrome (AIDS).

Ten immunocompromised men (9 with a diagnosis of AIDS and 1 with angioimmunoblastic lymphadenopathy with dysgammaglobulinemia (AILD)) with CMV retinitis were treated with a new anti-viral agent, trisodium phosphonoformate hexahydrate (Foscarnet). This compound has potent in vitro anti-viral activity against the entire Herpes group.

On therapy, all 10 patients had improvement or stabilization of their eye disease, and in 5 patients (50%) the retinitis resolved completely. The drug was well tolerated in most patients but minor adverse effects were frequent. Four patients experienced a rise in serum creatinine necessitating discontinuation of the drug. Confounding medications and infections contributed to this rise. No patient developed neutropenia on the drug. Recurrence of CMV retinitis occurred in 6 of 8 (75%) surviving patients, usually within one month of stopping therapy. One patient died 22 weeks after Foscarnet was discontinued without a recurrence. In 3 patients, the retinitis responded to subsequent courses of Foscarnet. One patient stabilized during an intermittent maintenance course of therapy.

We conclude that Foscarnet is an effective agent for the treatment of CMV retinitis and appears to be less toxic than previously described agents. The need for continuous intravenous infusion is its major drawback. Further evaluation is necessary to determine whether prolonged remissions can be achieved with intermittent maintenance therapy.

TH.8.2 Detection of Cytomegalovirus-Immediate Early Antigens in Blood Leucocytes as a Marker for Activity of Cytomegalovirus Infections in AIDS.

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Eight patients with AIDS were longitudinally studied on 57 occasions by detection of Cytomegalovirus (CMV)-immediate early antigens (IEA) in peripheral blood leucocytes. CMV-IEA detection was done by direct staining of leucocyte preparations in an immunoperoxidase assay, using monoclonal antibodies against the major CMV immediate early proteins. Simultaneously viral cultures of the blood buffy coat were done. CMV-IEA positive leucocytes, mainly neutrophils, characterized by a nuclear staining, were found in 38 of the 57 samples (67%). Twenty four of 57 blood cultures were positive for CMV (42%):23 (96%) were in the 38 CMV-IEA positive samples (61%).

The CMV-IEA assay was semiquantified in negative, low, intermediate and high levels of positive cells. Buffy coat cultures were only once positive at a negative CMV-IEA level (1/19), often (12/26) positive at low levels and nearly always positive at intermediate and high levels (11/12). Clinically disseminated CMV-disease correlated only with intermediate and high levels of positive cells and responded to antiviral therapy (DHPG), resulting in negative CMV-IEA tests and buffy coat cultures.

Conclusion: the CMV-IEA test seems to be a measure of CMV-viraemia in AIDS patients and might help in therapy decision making. The test can be performed in 3 hours.

TH.8.3 "Cytomegalovirus" Colitis: can it be caused by Adenovirus?
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Although commonly isolated from patients with AIDS adenovirus has previously been considered to be non-pathogenic. We suggest that this virus may be the cause of colitis indistinguishable clinically and histologically from cytomegalovirus disease.

The evidence is as follows: we have shown that isolation of adenovirus from any site is more common in patients with colitis than in those with disease at other organ sites, and adenovirus isolation rates from rectal biopsies/swabs in such patients are very high; although co-infection with CMV is common we have documented 2 cases of colitis where adenovirus was the only relevant pathogen isolated from any site at any time during the illness; histology of rectal biopsies from these patients has shown inclusion bodies "typical" of CMV. However culture of the same sample revealed adenovirus only, and electron microscopy of the inclusions demonstrated localised virus particles of ~70nm in size (adenovirus characteristically being 65-80nm) which are unlikely to be CMV (~100nm); the patients described have shown clinical and virological response to DHPG (an anti-CMV agent to which adenovirus is also sensitive at the normal therapeutic levels of 46-56μM achieved in both these patients, personal communication S.Tyms); clinical relapse was associated with recurrence of the adenovirus infection. Immunohistology and in-situ hybridisation studies of inclusion bodies in colitis are in progress and will confirm whether this is a common condition in AIDS patients.

TH.8.4 Zoster-associated Meningitis in HIV-infected Individuals
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Over an 18 month period, 7 patients in a cohort of approximately 150 HIV infected individuals developed dermatomal Herpes zoster. Of these 7, 5 had the onset of severe headache and fever within 4 days of the appearance of cutaneous lesions. Three subjects had previously been diagnosed with AIDS, while 2 had other HIV-related illnesses. Examination revealed meningismus in 4 patients and normal cognitive function and neurological examination in all 5. CSF abnormalities were consistently seen, with leukocyte counts of 14-128/mm^3 and protein of 89-256mg/dl (nml < 50). Varicella-zoster (VZ) was recovered from CSF in 2 subjects. HIV was recovered from cell-free CSF of 1 of 2 individuals in whom isolation was attempted, including 1 man who also had VZ in CSF. All 5 patients began to resolve their illness and CSF abnormalities within 3 days of beginning high dose intravenous acyclovir.

One possible explanation of these observations is that dermatomal VZ triggers HIV-associated meningitis. However, the apparent clinical response to acyclovir and recovery of VZ directly from CSF in several cases suggest an etiologic role for this virus. The degree of clinical illness and height of pleocytosis differentiate this illness from the mild pleocytosis sometimes seen with dermatomal zoster. The high frequency of this complication in our patients and the absence of encephalitis differentiate this entity from neurological complications of VZ in other immunocompromised patients. Thus, HIV infection appears to predispose to this specific complication of VZ. This potentially treatable form of meningitis should be considered when HIV-infected individuals present with headache and a vesicular exanthem.

TH.8.5 Disseminated Ecthymatous Varicella Zoster in AIDS
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Herpesvirus infections are among the most common and debilitating opportunistic infections in AIDS patients, and they may present atypically. We describe 3 AIDS patients who developed a solitary painful ulcerated cutaneous nodule followed by disseminated ulcerative cutaneous lesions which were found to be due to varicella zoster (2 definite, 1 probable). At no time were any vesicles seen. One case occurred in a patient with extensive eczema. Diagnosis was made by histology and viral culture of biopsy material. All cases responded well to acyclovir. This form of varicella zoster has not previously been described in either immunocompetent or immunosuppressed hosts, bearing little resemblance to either dermatomal zoster with dissemination or primary varicella. The profound loss of helper T cell function in AIDS may lead to multiple abnormalities in local immune response to cutaneous herpesvirus infections, and may be responsible for the atypical morphology and indolent course.

TH.8.6 Intrathecal Production of Antibodies Against T. gondii in Patients with Toxoplasmic Encephalitis and AIDS.
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Toxoplasma encephalitis (TE) has been recognized as a major cause of central nervous system (CNS) infection in patients with the acquired immunodeficiency syndrome (AIDS). The definitive diagnosis is difficult and sometimes requires the use of surgical procedures. Because of this we attempted to demonstrate local production, in the CNS, of antibodies to T. gondii and to determine the usefulness of these antibodies for the diagnosis of TE. We examined 22 patients with AIDS and TE and 12 patients with AIDS and non-toxoplasmic encephalitis. Antibodies to T. gondii were determined by using the DS IgM ELISA and the Dye Test (DT). Paired serum and cerebro spinal fluid (CSF) from each patient were used to determine intrathecal synthesis of antibodies. DT titers in serum and CSF as well as the total concentrations of IgG in these body fluids were used to determine production of specific IgG to T. gondii in the brain.

All patients had serum IgG but not IgM antibodies to T. gondii. Intrathecal synthesis of IgG was significantly higher in all patients studied. Local production of antibodies to T. gondii was noted in 10 of 13 patients with TE but only in 1 of 7 patients of the control group.

Our results suggest that demonstration of local production of T. gondii antibodies in the CNS may be useful for the diagnosis of TE in the appropriate clinical setting.

Immunology—HIV-Specific Antibodies

TH.9.1 HTLV-III(HIV) Synthetic Peptides: Generation of Murine Monoclonal Antibodies (MAb) and Analysis of Human Antibody Responses.
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Antibodies (Abs) to specific regions of viral proteins will have utility in mapping functional domains of such proteins. Furthermore, such Ab reagents can be used to probe for the presence of intact or degraded viral antigens. We have used synthetic peptides conjugated to immunogenic carrier proteins to develop MAbs to HTLV-III(HIV). MAb 2549 is specific for HTLV-3B envelope gp 120 (amino acids (aa's) 482-493, M R D N W R S E L Y K Y). In Western blots (WB) it reacts with gp160/120 and with two other components of Mr=40.5 and 43.5Kd from disrupted purified virus. Comparable extracts of noninfected H9 cells were unreactive. MAb 2549 specifically stained H9 cells infected with the RF or 3B strains of HTLV-III in indirect immunofluorescence assays, but did not inhibit HTLV-3B virus replication in neutralization assays.

ELISA analyses were performed on various synthetic peptides or peptide carrier conjugates using twenty human sera from apparently well blood donors positive for antibody to HTLV-3B by WB and by ELISA with viral lysates (Du Pont). Nine of these 20 positive sera were reactive with gp120 by WB. None of these reacted with peptide aa's 482-493, 474-487, and 488-502 in ELISA, but 8 of these 9 positive sera reacted with a proximal c-terminal gp120 peptide (aa's 503-518,).

These results show that synthetic peptides will aid in the mapping of human antibody responses to HTLV-III(HIV) antigens and that MAbs to specific viral protein regions make excellent controls for WB analyses.

TH.9.2 Immunodominant Epitopes of HIV Envelope Glycoproteins.
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A computer program was used to predict the epitopes of HIV envelope glycoproteins which are highly immunogenic. Both hydrophilicity and interactions between amino acids were used to calculate which regions of the folded native proteins are exposed on their outer surfaces for immune recognition by antibodies or T cells. Nine major immunodominant regions were identified. Comparison of amino acid sequences among HIV isolates revealed that 5 of these regions contain epitopes which are conserved. Peptides constituting highly conserved epitopes were synthesized and purifed by reverse-phase HPLC. Serum antibodies from some HIV-seropositive men but not from any HIV-seronegative men which recognize these peptides were demonstrated by ELISA, providing evidence of the antigenicity of these peptides. Antibody reactivity to these peptides in asymptomatic individuals and ARC, LAS, or AIDS patients was compared. The specific immunogenicity of these peptides was demonstrated by ELISA analysis of sera from peptide-immunized rabbits. Studies of the anti-viral effects of anti-peptide antibodies and the ability of these peptides to inhibit anti-CD4 monoclonal antibody binding are in progress.

TH.9.3 A Synthetic Peptide Derived from the Viral gp41 Protein of HIV is Highly Immunoreactive with Sera from Patients Infected with HIV

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A model for the transmembrane orientation of gp41 protein of HIV was proposed based on our computer analysis (LSAP). According to this model there are three transmembrane regions in gp41. Between two transmembrane sequences there is a loop on the surface of the virus membrane. This loop region is highly conserved between different HIV strains. To verify this model several peptides were synthesized from the loop region and transmembrane regions and polyclonal antibodies raised against these peptides. Peptides were tested in EIA with HIV-infected patients sera. None of the selected peptides from transmembrane regions were immunoreactive with sera from HIV-infected patients, whereas one of the selected peptides from the loop region (14 amino acids in length) was highly immunoreactive. All 50 serum samples tested, which were positive in both commercially available whole virus HIV-EIA and Western blot analysis, reacted with this peptide, indicating that this loop region is highly immunogenic. The specificity of this peptide to distinguish between positive and negative serum samples (1000 tested) was high (99,7 %). According to our preliminary results this peptide do not react with HIV-2/LAV2 positive sera.

TH.9.4 Antisera to Leu 3a with anti-idiotypic activity react with gp110/130 of HIV-1 and LAV-2

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The CD4 antigen is an essential part of the receptor for the human immunodeficiency viruses HIV-1 and LAV-2 (HIV-2) and binds directly to the envelope glycoprotein. Although there is virtually no cross-reactivity between these viruses when tested with sera from infected patients, both can be inhibited from interacting with CD4 by monoclonal antibodies (Mabs) to the same or very similar epitopes of CD4. Mabs to 2 distinct epitopes of CD4 were used to immunise mice to raise anti-idiotypic (anti-id) reagents which might react with the surface glycoproteins of these viruses. Antisera from 2 mice to one CD4 Mab (MT151) had strong anti-id activity as demonstrated by binding to the idiotype (id), but did not react with HIV by immunofluorescence, radio immunoprecipitation (RIPA) or a neutralisation assay. Antisera to Leu 3a, however, had strong anti-id activity, specifically stained the HIV infected cell line CEM, reacted with the gp110 of HIV-1 isolates CBL1 and RF and gp130 of LAV-2 by RIPA, and blocked syncytium formation between a CD4 bearing cell line and a HIV producing line. The antisera to Leu 3a strongly inhibited binding of labelled Leu 3a to CD4, but did not react at all with CD4 in competition studies or immunofluorescent staining. The antisera were unable to bind to a Mab (OKT4) directed to a different epitope of CD4, implying a private specificity. In conclusion, we have produced antisera with strong anti-id activity specific for Leu 3a. These react specifically with a conserved region of the surface glycoprotein of divergent isolates of HIV-1 and LAV-2, and identify a potential neutralisation site on these molecules.

TH.9.5 Internal Image Anti-idiotypes Representative of Homobodies Mimic the CD4 Molecule and Bind Human Immunodeficiency Virus.

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Internal image or related epitope anti-idiotypic antibodies (anti-Id) that mimic specific ligands and bind receptors have been referred to as homobodies. A monoclonal anti-Id was generated against Leu-3A, a mouse monoclonal antibody (MoAb) specific for the CD4 molecule on human T-helper /inducer lymphocytes. The anti-Id demonstrates CD4 mimicry indicative of a homobody based on the following properties: (i) it reacted with Leu-3a and not a panel of irrelevant mouse MoAbs; (ii) it partially inhibited the staining of CD4+ T-cells by Leu-3a; (iii) it detected a common idiotype present on other CD4 MoAb which block HIV infection in vitro; (iv) it stained HIV infected, but not uninfected T-cells and; (v) it bound a recombinant gp160 peptide and reacted with a molecule of M_r 110-120 KD protein in Western blot. The anti-Id also partially neutralized HIV infection in vitro. Baboons (Papio Cynocephalus Anubis) were immunized with OKT4A. An anti-Id response was produced that bound HIV in commercial ELISA's and recombinant gp160 in a solid phase immunoassay. In addition, the baboon anti-Id reacted with an HIV infected T-cell line and its binding inhibited the immunofluorescence staining of CD4+ T-cells by Leu 3a and OKT4A suggesting the anti-Id recognized the antibody combining site of the anti-CD4 MoAbs. The possibility that the baboon anti-Id may possess in vitro neutralizing is currently being examined. These results support further studies of the use of idotypes and anti-idiotypes as a potential vaccine candidates for HIV.

TH.9.6 A comparison of the interaction of HIV-1 and LAV-2 with the CD4 antigen.

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LAV-2 is a retrovirus isolated from individuals with an AIDS-like disease in West Africa. It is related to HIV-1 morphologically but these viruses have very little or no serological cross-reactivity in the envelope glycoprotein when tested with sera from infected patients. The CD4 antigen is an important part of the receptor for both HIV-1 and LAV-2, and the virus-receptor interaction can be blocked by monoclonal antibodies (Mabs) to different epitopes of CD4. We show here that the same or very similar CD4 Mabs which specifically inhibit the formation of syncytia between cell lines infected with various isolates of HIV-1 and CD4 bearing target cells, also inhibit in this assay with LAV-2. Similar results have also been obtained in an infectivity assay, in which HIV-1 or LAV-2 containing supernatant are used to infect CD4 bearing peripheral lymphocytes which have been pre-incubated with CD4 Mabs at varying concentrations. Reverse transcriptase (RT) values are then determined at various times after infection. Preliminary data from these experiments suggest that LAV-2 may bind with a higher affinity than HIV-1 to CD4. The inference from these results is that the binding site on these viruses is conserved, and since there is negligable serological cross-reactivity between antisera to these viruses, we conclude that the binding site is: a) not accessible to the immune system; b) non-immunogenic, or; c) a forbidden specificity. The implications for the preparation of a vaccine will be discussed.

Blood and Blood Products—Transfusion Associated AIDS and Hemophilia

TH.10.1 Transfusion-Associated AIDS in the United States

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We evaluated reported cases of transfusion-associated (TA) AIDS to characterize the natural history of HIV infection, estimate the magnitude of the epidemic, and monitor the effectiveness of HIV antibody screening. As of January 15, 1987, 570 TA-AIDS cases had been reported to CDC from 40 states. Males outnumber females by about 2:1 in every age group except 21 to 40-year-olds, for whom the ratio is 1:1. The mean incubation period is shorter for children aged < 13 years (mean 24 months) than for adults (36 months, $p<0.001$), but it is too early to detect cases with incubation periods > 9 years. Mathematical modeling had estimated the mean incubation period for adults will be 5 years, but current data suggest it will be longer. Because of the long incubation period, the incidence of TA-AIDS continues to increase in all age groups. No TA-AIDS cases have been reported in recipients of blood screened for HIV antibody whereas 10 TA-AIDS patients reported receiving their transfusions in the first 4 months of 1985. We estimate that 10,000 persons in the United States have TA HIV infections. Our study of families of adults with TA-AIDS found 38% had steady sexual partners, and transmission had occurred to 16% of the females and 8% of the males. If these estimates are generalized to all infected persons, 3,800 infected persons may be involved in sexual relationships, and 450 may have already transmitted infection. For 10 reported AIDS patients, the only risk for infection appears to be perinatal or sexual contact with an infected transfusion recipient. Secondary transmission from previously infected recipients may now be occurring more often than transmission by transfusion.

TH.10.2 The Transfusion Safety Study

JAMES W. MOSLEY*, THE TRANSFUSION SAFETY STUDY GROUP* **, *USC School of Medicine, Los Angeles, CA, **other participating institutions.

The Transfusion Safety Study (TSS) is a multifaceted, cooperative evaluation of factors influencing risk of transfusion-transmitted HIV infection, and interactions associated with progression. Subject groups include: (1) Persons in the 4 highest prevalence areas of the United States who donated blood in September, 1984, through January, 1985, just prior to routine donor screening; (2) recipients of components from anti-HIV(+) and (-) donors; (3) patients with congenital clotting disorders (CCD) receiving concentrates and components; (4) patients with congenital anemias (CA) receiving large numbers of transfusions; (5) untransfused subjects with CCD or CA; and (6) household contacts of treated subjects having CCD or CA.

Findings to date include: (1) The estimated prevalence of anti-HIV positivity among donors was 10 to 20 per 10,000 at the time of the survey; (2) homosexual contact was overwhelmingly the most important risk factor among donors; (3) 89% of recipients of anti-HIV(+) components have become anti-HIV(+); (4) there is a large difference in anti-HIV positivity associated with Factor VIII and Factor IX concentrates (78 vs 44%); (5) only 20% of CCD subjects treated just with components are anti-HIV(+); (6) only 6% of heavily transfused CA subjects are anti-HIV(+), and these cases are confined to high prevalence areas; (7) 17% and 0% of sexual and non-sexual household contacts of anti-HIV(+) CCD and CA have become seropositive; (8) no seroconversion of any subject has been observed on follow-up. (Supported by Contracts No. NO1-HB-4-7002 and NO1-HB-4-7003 of the National Heart, Lung, and Blood Institute.)

TH.10.3 Clinical Observations on HIV Seropositive Hemophiliacs after 4 1/2 Years of Followup and Efficacy of Heat-treated Products.

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Individuals with hemophilia represent one of the four major groups at risk for developing acquired immunodeficiency syndrome (AIDS) because of their use of blood products. The majority of hemophiliacs seroconverted to human immunodeficiency virus (HIV) by late 1982. We have been prospectively following a group of 84 hemophiliacs since July 1982. All were healthy and asymptomatic at that time. Our results show the following:

		HIV Positive			HIV Negative
Factor	Total	Asymptomatic	AIDS	ARC	Total
VIII	45	36	4	5	14
IX	10	9	0	1	15

Of the factor VIII patients, 11% have developed AIDS and died during the past 4 1/2 years, and 9% have developed ARC. Of the factor IX patients, 10% have developed AIDS and died; none have symptoms of ARC. In 1984, all of the seronegative patients were switched to factor VIII and IX concentrates that had been heated at 60 or 68° for 72-77 hours, and all have remained seronegative and asymptomatic for 2 1/2 years. These patients have received 1000 - 100,000 units of the concentrates. These results indicate that in 4 1/2 years 11% of seropositive hemophiliac patients have developed AIDS and 7%, ARC. These results also document the efficacy of heat-treatment at 60° or 68° for 72-77 hours in eliminating HIV from factor VIII and IX concentrates.

TH.10.4 No Anti-HIV Seroconversion after Replacement Therapy with Pasteurized F VIII Concentrate. A Study of 151 Patients with Hemophilia A or von Willebrand's Disease.

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Transmission of hepatitis viruses and HIV has proven to be a risk of replacement therapy in hemophilia. As regards F VIII products a concentrate (Hemate HS or P) in which viruses are inactivated by heat-treatment over 10 hours at 60° C in aqueous solution is available since 1979. Our clinical studies have shown that this product does not transmit HBV and HNANBV. As the product was manufactured by 80% from US plasma it was necessary to prove that it also does not transmit HIV. As it is, for ethical reasons, not possible to treat a control group with non-virus-inactivated F VIII, non-transmission of HIV can only be proven if anti-HIV seroconversion does not occur in larger groups of patients treated exclusively with this virus-inactivated product. We collected data from 151 patients treated with Hemate HS (P) who had never before received blood or blood products. Therapy was started between Feb. 1979 and Jan. 1986 (median July 7, 1983). The median length of observation till the last anti-HIV testing was 24 (3 - 83) months, the median total dosage was 17,000 (500 - 2,155,375) IU of F VIII, the median patient age was 6 (0,5 - 68) years. In none of these patients anti-HIV seroconversion (ELISA test) was observed. According to the rule of three, the upper 95% confidence limit for a random sample of 60 cases with zero events would be 3/60 or 5%. For greater numbers of n cases, as in our study, the range of confidence narrows increasingly. The period of observation of this study is hitherto the longest.

TH.10.5 Antibodies to HIV in Israeli Hemophiliacs: Prognostic Significance of Serological Profile

SHLOMIT ORGAD*, G. MALONE**, R. ZAIZOV***, U. MARTINIWITZ*, E. GAZIT*, M. ESSEX**, *Sheba Medical Center, ISRAEL, **Harvard School of Public Health, Boston, MA, ***Beilinson Medical Center, ISRAEL.

We studied 66 Israeli hemophiliacs for antibodies to HIV on blood samples collected between 1978 to 1985. By May 1985, 2 had AIDS, 2 had ARC, 4 had lymphadenopathy, and 58 were asymptomatic. Antibodies to HIV were detected in 40 (60.6%) patients. Presence of HIV antibodies was significantly associated with receipt of non-heat-treated commercial factor VIII concentrates (NHT.Fac.VIII) between 1980 to 1983. 84.44% of patients treated with NHT.Fac.VIII developed antibodies, compared to 25% treated with cryoprecipitates and fresh plasma only. All 40 seropositive patients had antibodies to viral env gene encoded gp120/gp160 antigens. Twenty-four (60.0%) also had antibodies to viral gag gene encoded p24 and/or p55 antigens. While antibodies to gp120/160 persisted during the follow-up time, a loss of antibodies to p24/55 was observed in 25% of seropositive patients from whom multiple samples were available. Gp120/160 positive p24/55 negative hemophiliacs had significantly lower absolute T-helper cell counts and reversed Th,Ts ratios compared to gp120/160, p24/55 seropositive patients. Four of 16 (25.0%) asymptomatic gp120/160 positive p24/55 negative patients developed overt disease within 15 months of the last blood collection. The data suggest that antibodies to gp120/160 are of important diagnostic value while loss of antibodies to p24/p55 may be of prognostic value.

TH.10.6 Incidence of HIV-1 and HIV-2 antibodies in hemophiliacs

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The presence of antibodies to HIV-1 (anti-HIV-1) in a group of hemophiliacs has been monitored since the autumn of 1984. Increasing numbers of HIV-1 infected patients were observed in the years 1981 to 1986 from 0 to 51% (85 patients of 166 positive for anti-HIV-1). Most infections occured between 1982 and 1984 and only 5 seroconversions were observed since 1985. Only heat or chemically inactivated clotting factor preparation were used for substitution of the patients since the spring of 1985. Two of the five seroconversions in 1985/86 may have been due to a factor VIII preparation inactivated by heat in the dry state and this preparation is no longer used. The other 3 seroconversions possibly were caused by an occasional use of an noninactivated preparation in the beginning of the change to inactivated clotting factor preparations. 38 of the anti-HIV-1 positive sera were tested also for the presence of anti-HIV-2 by an ELISA prepared in our own laboratory, immunofluorescence and immunoblot. HIV-2 (LAV-2) for these tests was kindly provided by L. Montagnier. Antibodies specific for HIV-2 antigens were not detected, but crossreactions were observed between anti-HIV-1 with HIV-2 antigens particularly epitopes on HIV-2-p27.

The data inidicate that the use of adequately inactivated clotting factors can prevent infection of hemophilia patients by this route and that HIV-2 was not present in the clotting factor preparations used for the substitution of this group of patients.

Health Care—Issues in Health Care Delivery

TH.11.1 Comprehensive outpatient-based healthcare reduces inpatient stay for persons with AIDS or ARC: the Los Angeles County Model.

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Patients with HIV infection have complex health-care needs. Several problems are perceived with hospital inpatient based programs: care for multiple AIDS diagnoses may be dispersed, acute-care services are used for convalescence, procedures require repeated admissions. We have previously reported the cycle of new symptoms, procedure-oriented diagnosis and treatment is more frequent for persons with AIDS than other chronic illnesses and results in an average of 2.3 inpatient admissions/patient/year. As the number of HIV infected persons seeking medical attention increases, alternatives to inpatient care are needed. We examined the effect of an outpatient-based program on the use of acute-care inpatient resources by persons with AIDS or ARC. Each new patient was assigned a physician supervised, primary care nurse and social worker outpatient team (PCT) which coordinated all clinic visits. Physician specialists varied with time based on the patient's AIDS diagnoses. Over two years of study, a strong inverse correlation was noted between the number of monthly outpatient visits and inpatient length of stay (LOS). Reasons for admissions when regular clinic visits were not planned or available included diagnostic tests, hydration, drug infusions and psychosocial support. Reduction of LOS was associated with significant reduction in charges/patient served. This study supports the hypothesis that an outpatient-based PCT case-management strategy reduces LOS and charges for persons with AIDS/ARC and may prove to be more flexible in meeting increased demand and patient satisfaction.

TH.11.2 Hospital Utilization Patterns and Charges for the Care of Inner City AIDS Patients: By Risk Group, Sex & Race/Ethnicity

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The hospital records for 39 AIDS patients who received all of their inpatient care at Montefiore between August 1981 and June 1986, were examined to determine patterns of utilization (length of stay (LOS) and number of admissions); charges (room, board and ancillary services); and the relationship of these to patient characteristics. Sixty percent of the patients had a history of intravenous drug abuse (IVDA); 40% were women; 30% were Black; 44% Hispanic; 25% White. Overall, these patients had a mean survival time of 7.75 months after diagnosis (range 3 days to 42 months), and averaged 3.2 admissions (1-18) of 17.6 days (11-186) each. The mean total LOS was 56.3 days, with total charges $41,484 per patient ($29,143 room & board; $12,341 ancillary services). IVDA's did not differ from non-IVDA's in number of admissions, LOS or charges. Women had fewer hospital admissions (2.4 vs. 3.8); shorter per patient total LOS (44.4 vs. 64.7 days); and, accordingly, lower total charges ($33,514 vs. $46,038). These differences (n.s.) were attributable to those 19 patients diagnosed prior to July 1984 when women had a significantly shorter interval between diagnosis and death than men (3.7 vs. 14.2 months, p= .001). Black patients had a shorter total LOS than Whites and Hispanics (38.3 vs. 66.1 days, n.s.), and this trend held when stratified for sex and risk group. These findings show total hospital LOS and costs to be considerably higher than a recent comparable lifetime cost study of primarily homosexual patients in San Francisco (Scitovsky, et.al., JAMA, 1986).

TH.11.3 Medical Care Costs of Children with HIV Infection in Harlem
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We have examined the costs of medical care for infants diagnosed with HIV infection at Harlem Hospital (N = 33). From a careful review of patient charts, a total utilization of medical resources was determined and assigned a cost value. The cost value was determined independently from charge-based billing records and standardized to Medicare reimbursement figures whenever possible. The costs of caring for these infants range form $250 to $700 per day. This wide range reflects the variation in resource utilization exhibited by asymptomatic infants (Ab+) versus infants with ARC or AIDS.

What is common to all of these infants are lengthy hospital stays as a result of the current absence of viable placement alternatives to the home or hospital. Once admitted, these infants may never leave the hospital regardless of medical need. The mean length-of-stay for nine of the unplaced infants was 280 days and will exceed one year in April 1987. Our study demonstrates that the individual cost of care for several infants has already exceeded $300,000 after more than one year of hospitalization.

A recent study reported that the lifetime cost of AIDS in adult patients averages $733 per day over a total hospitalization of 37.6 days for a cumulative mean cost of $25,571.[1] These data for adult patients sharply contrast with our findings for the medical costs accrued by pediatric HIV infected patients at Harlem Hospital. The potential expense of caring for these children in our city hospitals is enormous. [1Scitovsky, A. et.al. JAMA (vol. 256, no. 22) December 12, 1986.]

TH.11.4 AIDS Medical Day Care for Intravenous Drug Abusers
GLORIA RODRIGUEZ, J. JACKSON, N.J. State Department of Health, East Orange, N.J. AIDS Community Support Unit

New Jersey presently ranks fifth nationally in the number of confirmed AIDS cases. As of Dec. 1, 1986, this number had risen to 1,709 with an overall mortality rate of 61%. Of special significance is that 52% of the total number of cases are intravenous drug abusers. Presently, chronic long term care facilities and extensive home health care are not available. Consequently many AIDS/ARC patients must remain hospitalized at considerable cost. Comprehensive cost-effective specialized services must be created and made accessible in order to meet the multiple needs of the AIDS/ARC patient. The AIDS/ARC Medical Day Care Program addresses the needs of recipients of the N.J. Medicaid Program who could benefit from a health service alternative to institutionalization. AIDS Medical Day Care is a program of medically supervised, health related services in an ambulatory structured drug treatment program setting to persons who do not require 24 hours in-patient institutional care and yet, due to their physical and/or mental impairment, need supportive health maintenance and restorative services. Services provided include medical, nursing, social, transportation, personal care, dietary, recreational, rehabilitative, drug counseling and dental. The structured drug treatment setting meets their needs, helps reduce transmission, provides a cost effective, humane mode of health care and enables IVDA AIDS patients to remain in the community.

TH.11.5 A Hospital-based Volunteer Program Utilizing Methadone Patients and Others to Provide Support for Inner-city AIDS Patients
LEA TENNERIELLO, M. CALLAN, L. GORDON, J. LEVINE, B. POUST, E. DRUCKER, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA

We report the initial six-months of a hospital-based Volunteer Program designed to serve a patient population of predominantly minority backgrounds, low socioeconomic status, and minimal personal support systems: 56% are intravenous drug abusers; 10% are heterosexual partners; and 35% are gay men. The volunteer population mirrors the composition of this patient group and 50% are patients in our Methadone Program. As of February 1987, 20 volunteers had completed a 2-day training program and attend weekly volunteer support groups with professional supervision of their individual work. Volunteers have provided over 1000 hours of service to over 30 different patients and have organized large Thanksgiving and Christmas celebrations for hospitalized patients. The Project's successes include: the establishment of a positive working coalition of volunteers from diverse backgrounds; the use of Methadone patients (often stereotyped, discounted and self-disparaging) to help the AIDS community while increasing their own self-worth; the creation of a strong source of group support and breavement consolation for survivors of deceased patients. Program difficulties include: recruitment and selection of appropriate volunteers from a population which includes many multi-problem, poorly functioning persons; the need for safeguards against destructive experiences for patients and volunteers; adaptation of the training program and supervision to the needs of the volunteers and the hospital; and securing adequate funding for the project. The paper describes in detail the process of screening, training, on-going support and supervision of volunteers and discusses plans for future expansion.

TH.11.6 Hospice Care of Intravenous Drug Abuser AIDS Patients in a Skilled Nursing Facility.
W BULKIN, L MCNALLY, G MCGUIRE, L BROWN, GH FRIEDLAND. Beth Abraham Hospital, Montefiore Medical Center/Albert Einstein Coll. of Med., Bx., N.Y., USA.

Thirty two percent of AIDS patients in NYC are intravenous drug abusers (IVDA). Hospice care for AIDS patients in NYC has been limited and there is no previous experience with IVDAs with terminal illness in this setting. We report on the initial experience in hospice care for a predominately IVDA AIDS population at a Skilled Nursing Facility (SNF) with a Certified Hospice Program delivering home care and inpatient care.

To familiarize staff with AIDS issues, a staged educational program preceded patient admission. Between Feb. 1986 and Jan. 1987, 80 patients were referred and 30 were accepted. Of these 22 were male, 8 female. 20 were IVDA, 7 homosexual men, 2 sex partners of IVDA, 1 unknown. Mean age 35, all 30 had AIDS dementia complex. Total days of hospice care 867, mean length of stay 30 days (range 1-280). 88% days spent in inpatient hospice care, only 12% in home hospice care. Mean daily inpatient census, 4.

Based on daily rate of $758 for acute hospital care and $346 for hospice care, estimated savings in decreased costs for 12 months, $357,204. Compared to other hospice patients, unanticipated problems included: (1) inability to provide home hospice care because of inadequate or absent housing and IVDA related social disruption, (2) continuing drug abuse, (3) increased nursing, medication, psychosocial needs, (4) difficult interactions with funeral directors. Continuing fear of transmission among staff was not a major problem.

Hospice care of AIDS patients in a SNF is feasible, humane and cost effective. However, problems of IVDA require special attention and program modifications, if hospice care is to be provided for this population.

Roundtable Discussions

TH.12

People Living with AIDS: Personal Perspectives

Panel Organized By: Stephen Beck
National Association of People with AIDS
Washington, D.C.

Panel Moderator: Frederick Garnett
National Association of People with AIDS
Washington, D.C.

People of Color with AIDS

IV Drug Users with AIDS

Women with AIDS

Canadian PWAs

European PWAs

Caribbean PWAs

TH.13

Prevention of Perinatal Transmission of HIV Infection

Panel Moderator: James Allen
Centers for Disease Control
Atlanta, Georgia

Jeffrey P. Davis, Wisconsin Department of Health and Social Services, Madison, Wisconsin

Howard Minkoff, Downstate Medical Center, SUNY, Brooklyn, New York

Janet Mitchell, Beth Israel Hospital, Boston, Massachusetts

James Oleske, St. Michael's Medical Center, Newark, New Jersey

Gwendlyn B. Scott, University of Miami School of Medicine, Miami, Florida

Pauline A. Thomas, New York City Department of Health, New York, New York

TH.14

AIDS Education for the General Public

Panel Moderator: Paul Kawata
National AIDS Network
Washington, D.C.

Hillary Pickles, Department of Health and Social Security, London, England

Walter Dowdle, Centers for Disease Control, Atlanta, Georgia

Jan-Olog Morfeldt, National Bacteriological Laboratory, Stockholm, Sweden

Carol Sussman, American Red Cross, Washington, D.C.

TH.15

AIDS in the Developing World (Social/Economic)

Panel Moderators: Bradshaw Langmaid
Agency for International Development
Washington, D.C.

Lair G.M. Rodrigues
National AIDS Program
Brasilia, Brazil

Oleh Wolowyna, Research Triangle Institute, Research Triangle Park, North Carolina

Dr. Benjamin Were, Kenya Medical Research Institute, Nairobi, Kenya

Charles Meyers, Harvard Institute for International Development, Cambridge, Massachusetts

Michael Micklin, Florida State University, Tallahassee, Florida

V. Ramalingaswami, Harvard School of Public Health, Cambridge, Massachusetts

TH.16

Hemophilia: Where Should the Preventive Effort Be Placed?

Panel Moderator: Peter Levine
Worcester Memorial Hospital and
University of Massachusetts Medical School and
New England Area Comprehensive Medical Center
Worcester, Massachusetts

Peggy Heine, The National Hemophilia Foundation, New York, New York

Jean-Pierre Allain, Abbott Laboratories, Abbott Park, Illinois

Piero M. Mannucci, University of Milan Hemophilia Center, Milan, Italy

TH.17

Current Issues in Drug Abuse and AIDS

Panel Organized By: Peter Bridge
Department of Health and Human Services
Bethesda, Maryland

Panel Chairman: Roy Pickens
NIDA
Bethesda, Maryland

John Newmeyer, University of California, San Francisco, San Francisco, California

Don Des Jarlais, New York State Division of Substance Abuse Services, New York, New York

Jerome Jaffe, NIDA, ARC, Baltimore, Maryland

George Bigelow, Johns Hopkins University, Baltimore, Maryland

Poster Session

THP.1 Select Lectins Inactivate HIV In Vitro. W. EDWARD ROBINSON, DAVID C. MONTEFIORI AND WILLIAM M. MITCHELL, Vanderbilt University, Nashville, Tennessee, USA.

To evaluate the potential role of oligosaccharides in the attachment of HIV to the T4 receptor, we examined the effect of several lectins on viral infectivity. Lectins tested were BS-II, lentil, wheat germ agglutinin (WGA), hairy vetch, red marine algae, phytohemagglutinin-P (PHA), concanavalin-A (Con-A), and succinyl concanavalin-A (sCon-A). We found that at 500 nM concentrations Con-A and sCon-A preincubated with virus completely inhibited virus expression in target C3 cells as determined by indirect immunofluorescence (IIF) and reverse transcriptase assay (RT). Lentil and PHA greatly diminished viral infectivity (IIF and RT $<20\%$ of control) while WGA only slightly inhibited the virus (RT and IIF $<60\%$ of control). BS-II, hairy vetch, and red marine algae failed to inactivate the virus at all (RT and IIF $>80\%$ of control). We further found that monovalent sCon-A can prevent HIV infection of target cells significantly at a concentration of 400 nM. Since there is no relationship between lectin size and degree of inhibition of HIV infectibility, the observed antiviral activity appears to be related to lectin oligosaccharide specificity rather than simple, non-specific stearic hindrance. Thus, these findings indicate that the oligosaccharide side chains of the HIV envelope proteins may be involved in the attachment of the virus to the T4 receptor of T-helper lymphocytes and that modulation of HIV oligosaccharides may be a useful target for the development of chemical anti-HIV agents.

THP.2 A Rapid and Convenient Detection of HIV by in situ Hybridization Using Non-Isotopically-Labelled Probes

KEVIN S. BYRON, SUSANNE M. SCESNEY, JOHN L. SULLIVAN and ROBERT H. SINGER*, U. Mass. Medical School, Pediatrics and Anatomy*, Worcester, MA 01605

We have developed an in situ hybridization methodology for rapid detection of HIV in infected cells using H9 or CEM cells as models. Cells were probed with a biotinylated DNA HIV probe followed by streptavidin and then biotinylated alkaline phosphatase (ABAP). An intense colorimetric reaction is generated in HIV-infected cells which can be easily distinguished at cell dilutions of 1×10^{-5}. When compared with isotopic probes, it was determined that the sensitivity of non-isotopic detection was comparable. Using both isotopic and non-isotopic probes we have detected HIV-infected cells in peripheral blood lymphocyte cultures within ten days of stimulation with PHA. S^{35}-labelled probe was more sensitive for low levels of infection, however, for routine viral isolation procedures the ABAP technique was several orders of magnitude more sensitive than reverse transcriptase assays or RNA dot blot hybridization. We are currently studying splenic mononuclear cells (obtained from an HIV-infected individual splenectomized for ITP) for direct visualization of HIV-infected cells using both detection systems. In addition to HIV detection in patient samples, we have used the ABAP technique to develop an HIV neutralization assay. This assay can be easily quantitated with stringent end-point titration of serum neutralizing antibody to HIV. These studies indicate that non-isotopic in situ hybridization for detection of HIV is a convenient and rapid method for clinical and research laboratory investigation of HIV infection. Supported by NIH Contract NO1-HB-67022

THP.3 Presence of Human B-Lymphotropic Virus (HBLV) Antibody in Sera from Infected AIDS Patients

OHARAM V. ABLASHI*, Z. SALAHUDDIN*, M. KAPLAN**, F. IMAM*, C. CAIN*, and R. GALLO*, *National Cancer Institute, Bethesda, MD, ** North Shore University Hospital Long Island, NY

We recently described the isolation of a novel herpesvirus (HBLV) from patients with lymphoproliferate disorders as well as from 2 patients with HTLV-III-related diseases. One hundred and twenty sera obtained from AIDS patients, 33 with lymphoma and 46 with Kaposi's Sarcoma (KS), were tested for antibody to HBLV by indirect immunofluorescence assay (IFA). Out of 120 sera from HTLV-III-related diseases, 31 contained IgG antibody to HBLV by IFA (25.8%). In addition to 220 sera from normal healthy individuals tested previously (4 contained HBLV antibody) for HBLV antibody, 80 additional normal sera were included in the present study. Among the 80 healthy donors, 6 sera were positive to HBLV (7.5%). Out of the 13 (39.3%) HBLV antibody-positive B-cell lymphomas sera, 4 exhibited strong IFA positivity to HBLV (1:40 dilutions), whereas the remainder of the positive sera were reactive at 1:20 dilution. Also, sera (32.6%) from KS patients were found to contain HBLV antibody. These results are consistent with the role of HBLV in lymphoproliferative disorders and/or diseases of the immune system, but much more information is needed to draw any conclusions.

THP.4 Immunological Detection of HIV-Infected Peripheral Blood Lymphocytes

RUDOLF O.F. KUNZE and M.A. KOCH, Robert Koch-Institut des Bundesgesundheitsamtes, 100 Berlin 65, F.R.G.

Virus antigen expressing cells can be detected by the APAAP-technique using a cocktail of murine monoclonal antibodies against viral p15, p24 and gp120. In freshly isolated peripheral blood mononuclear cells (PMC) from HIV infected persons only an occasional cell in 5000 will exhibit typical staining. If such cells are cultured for 3 days in the presence of PHA (1 ug/ml) HIV antigen positive cells are demonstrable regularly with a frequency of 1:1000 to 1:100. From the results of kinetic studies of in vitro HIV infected PMC it can be excluded that the HIV infected cells observed result from infection during in vitro cultivation, i.e. either the majority of cells expressing antigens after stimulation, produce without stimulation antigen below level of detection or are latently infected. Number of $CD4^+$ positive cells were determined for the same samples. On the assumption that only $CD4^+$ cells express viral antigens 1-10% of these cells are infected in the patients investigated. This suggests that number of virus bearing PMC is far greater than hitherto assumed. No correlation between number of infected cells and stage of disease was observed.

THP.5 MOLECULAR CLONING AND BIOLOGICAL ACTIVITY OF HUMAN T-LYMPHOTROPIC VIRUS TYPE-4.

Hardy Kornfeld, Norbert Riedel, Gregory Viglianti, Vanessa Hirsch and James I. Mullins. Department of Cancer Biology, Harvard School of Public Health, Boston, MA 02115, USA.

Using molecularly-cloned DNA of simian T-cell lymphotropic virus from an African Green monkey (STLV-3AGM) as probe, we examined the genetic relationship between individual isolates of STLV-3AGM, STLV-3 derived from macaques from the New England Primate Research Center, and HTLV-4. The consensus restriction site maps for all of these isolates differed at no more than 3/34 sites examined. Strong homology, but distinct restriction site patterns were detected in cell lines infected with STLV-3 from a sooty mangabey from the California Primate Research Center and a macaque isolate from the Delta Primate Research Center, possibly infected from a sooty mangabey.

Molecular clones of HTLV-4 were obtained and shown to encode transmissable virus which induced formation of giant multi-nucleated cells in HUT-78, but with minimal cytolysis. Infection could be blocked by pre-treating cells with anti-CD4 antibodies indicating that HTLV-4 likely employs the same receptor as HIV. Comparison of the STLV-3/HTLV-4 consensus with that of the LAV-2/HIV-2 reveals some restriction site conservation and sequence homology in the LTR considerably stronger than either sequence shares with HIV.

THP.6 In Vitro Mutagenesis of the HIV (HTLV III/LAV) Genome

ANDREW DAYTON*, JOSEPH POTZ*, BRUCE WALKER*, TATYANA DORFMAN*, and WILLIAM A. HASELTINE**.*Dana-Farber Cancer Institute, Dept. of Biochemical Pharmacology, Harvard Medical School, and **Harvard School of Public Health, Dept. of Cancer Biology, Boston, MA.

We have introduced a series of mutations into the HIV genome by random linker insertion mutagenesis. Our early work has concentrated on the effects of mutations in the integrase region of the genome, just 3' to the reverse transcriptase gene.

Cloned genomes with integrase mutations transiently synthesize a complement of viral proteins normal except for the lack of the integrase protein. These DNAs also transiently produce reverse-transcriptase-containing particles which are, however, defective for replication. Preliminary data suggests that these particles may be defective at a point past the formation of proviral DNA subsequent to infection. The results legitimize the integrase gene product as a potential therapeutic target.

THP.7 Clinical, Hematological, and Immunological Evaluation of Individuals Exposed to Human T-Lymphotropic Virus Type IV (HTLV-IV)

RICHARD G. MARLINK*, D. RICARD**, S. M'BOUP**, P. KANKI*, J.L. ROMET-LEMONNE*, M. ESSEX, et al., *Harvard School of Public Health, Boston, MA, **University of Dakar, Dakar, SENEGAL.

We studied various epidemiological and clinical parameters in over 300 prostitutes from Dakar, Senegal. Of this cohort, 7% were found to be seropositive for exposure to HTLV-IV as compared to a seropositive rate for the general population in Dakar of $\backsimeq$1.5%. All prostitutes were evaluated in a clinic which serves the medical needs of this population. Follow-up has been for greater than 18 months and the seropositive prostitutes have remained without significant lymphadenopathy, without a history of chronic fevers, diarrhea, pruritis, or weight loss, and without significant differences in cutaneous anergy when compared to prostitutes seronegative to HTLV-IV. The estimated number of lifetime sexual contacts was comparatively increased in the seropositive prostitutes, but serology to sexually transmitted diseases and/or endemic diseases including HTLV-I was not significantly correlated with HTLV-IV seropositivity.

Significant elevations of polyclonal IgG levels (p=.0001) and of absolute T8 lymphocyte counts (p=.04) were found among the HTLV-IV seropositive prostitutes when compared to seronegative prostitutes and to surgical controls from Dakar. Notably, both total T cell counts and absolute T4 cell counts showed an inverse correlation to age greater than 40 years in all 3 populations, regardless of serologic status. Other significant findings were the presence of immune complexes in at greater levels in sera of seropositive prostitutes, as well as elevated levels of B_2-microglobulin.

We conclude (1) that HTLV-IV is a sexually transmitted virus, (2) that certain immunologic parameters are consistent with a persistent viral infection, and (3) that the absence of abnormal clinical findings in this cohort over time is markedly distinct from similar cohorts exposed to HTLV-III/HIV in Central Africa and may represent reduced pathogenicity of HTLV-IV compared to HTLV-III/HIV.

THP.8 Anti-HIV Activity of 2',3'-Dideoxycytidine and the Unsaturated Derivative (2',3'-Dideoxy 2',3'dehydrocytidine) Compared to 3' Azidothymidine (AZT).

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Anti-HIV activities of 2',3'-dideoxy 2',3'-dehydrocytidine(ddd-C); 2',3'-dideoxycytidine(dd-C), and 3' azidothymidine(AZT) were compared in an infectivity assay which employs the LAV isolate of HIV to infect CEM cells. Virus production was monitored 15 days after infection by an EIA which uses a monoclonal antibody to capture viral core antigen (p25) and a polyclonal antiserum conjugated to HRP as signal.

The three compounds, when added 24 hours prior to infection at a concentration of 1 μM, inhibited production of detectable viral antigen when the virus inoculum was 50 TCID 50. When the inoculum was 500 TCID-50, viral antigen production in the presence of 0.5μM and 1μM AZT was 66% and 23%, respectively, of virus control antigen levels. In contrast, ddd-C at concentrations of 0.5μM and 1μM showed complete inhibition of viral antigen production. To determine the effect of these compounds after virus infection, an experiment was performed, allowing the virus to adsorb to the cells 45 minutes prior to the addition of the drugs. The results show that both dd-C and ddd-C at a concentration of 1μM inhibited viral antigen production completely, even when the virus inoculum was 500 TCID-50, while antigen production in the presence of 1μM AZT was 100% of virus control levels. This indicates that both dd-C and ddd-C are more effective inhibitors of HIV antigen production than AZT in both formats of this in vitro infectivity assay system.

Other compounds have been tested, and results will be discussed.

THP.9 Detection of HIV antigen and specific antibodies to HIV core and envelope proteins in sera of patients with HIV infection.

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We have tested clinically well characterized populations for 3 markers of HIV infection; HIV antigen (HIV Ag), p24, and gp41 antibodies (Ab) to HIV. Of 563 patients, 251 were from populations diagnosed as AIDS with opportunistic infections (AIDS-OI), AIDS with Kaposi's sarcoma (AIDS-KS) and ARC. 176 specimens were from high-risk asymptomatic individuals and 136 from control subjects or patients with non-AIDS related disease. None of the 136 control individuals that we tested were reactive for either HIV Ag, or HIV antibodies to p24 and gp41.

Of the 427 HIV seropositive individuals, 99 to 100% were reactive for gp41 Ab to HIV. In contrast, we found that the seroprevalence of p24 Ab to HIV varied from 23 to 83% and appeared to be inversely associated with the severity of clinical symptoms. When specimens were analyzed for the presence of HIV Ag, we observed that in seropositive individuals, the prevalence rate for this marker was lowest (1.4%) in asymptomatic individuals and highest (50%) in the AIDS-OI diagnosed group. Also, 240 cases with AIDS-KS, OI, ARC and high-risk asymptomatic individuals group were analyzed for T4 cell number and T4/T8 ratio; only one (2.0%) HIV Ag positive case showed a T4 cell number > 400 and a normal T4/T8 ratio.

These studies appear to demonstrate a direct correlation between the presence of HIV Ag and the severity of HIV infection illnesses. In one individual, HIV Ag was the only marker present, suggesting to us that in similar cases, the detection of HIV Ag may be the sole evidence for a biological diagnosis of HIV infection with current diagnostic procedures.

THP.10 Activity of dideoxynucleosides against HTLV-III/LAV in vitro in different human cells.

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Several dideoxynucleosides have been shown to have potent activity against HTLV-III/LAV in vitro in T cells. It has recently been shown that macrophages and Epstein-Barr virus (EBV)-infected B cells may be infected by HTLV-III/LAV; macrophages may be particularly important clinically. Dideoxynucleosides must undergo anabolic phosphorylation and the enzymes that mediate this may vary from cell to cell. We have examined the ability of several dideoxynucleosides to protect two macrophage lines (THP-1 and U-937) and two EBV-infected B cell lines (VDSO and HER) against infection with 3000 virions/cell of HTLV-III/LAV. Culture supernatants were examined for reverse transcriptase (RT) and HTLV-III/LAV p24 antigen. 2',3'-dideoxyadenosine (ddA) completely protected both VDSO and HER even at 5 to 10 uM. An IL-2 dependent T cell line derived from the same donor as HER, as well as the T cell lines ATH8 and H9, were also protected at concentrations down to 5 to 10 uM of ddA. Proliferation of these B and T cell lines was not affected at concentrations up to 50 uM. Thus, ddA is effective at protecting both EBV-transformed B cells and T cells. THP-1 and U-937 were completely protected against infection with HTLV-III by 0.2 uM of 2',3'-dideoxycytidine (ddC), while proliferation was not affected. THP-1 was also completely protected by 3'-azido-3'-deoxythymidine (AZT) at concentrations down to 0.5 uM, while U-937 was only 85% protected at a concentration of 10 uM. Studies of the phosphorylation of dideoxynucleosides in these lines are ongoing at present. These results indicate that while there may be some differences among these different human cell types, dideoxynucleosides can protect EBV-infected B cells and macrophage lines as well as T cells against infection by HTLV-III/LAV.

THP.11 Cytopathic Effects of the Human Immunodeficiency Virus do not Correlate Necessarily with Cell Fusion.

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To study the role of syncytium formation in the cytopathic effects of HIV infections on T4+ lymphoid cells, we followed the infection of an established laboratory stock of HIV, HTLV III, as well as a recent patient isolate, HIV(UMA-CB), on H9 cells, CEM cells, and peripheral blood lymphocyte (PBL) cultures. Virus spread and the onset of cytopathic effects were similar in each of the HIV-infected cultures. Unexpectedly, HIV-induced syncytia were not observed except in infected H9 cells with the peak occurence of syncytia preceding peak cytopathic effects in these cells. Mixing experiments and flow cytometry were used to determine whether cell-specific expression of HIV envelope glycoproteins or density of the T4 receptor determined susceptibility to HIV-induced fusion. The results of these experiments indicate that (i) actively infected cells that both do and do not undergo fusion express HIV envelope antigens which can initiate cell fusion, (ii) HIV-infected cells initiate syncytium formation more efficiently with uninfected than infected cells (presumably due to viral envelope glycoproteins interfering with the expression of T4 antigen in infected cells), and (iii) the apparent surface density of T4 on a T4+ lymphoid cell does not determine susceptibility to HIV-induced fusion. On the basis of these results it seems likely to us that the primary cause of T-cell loss in HIV-infected patients will not be the result of HIV-induced cell fusions and that T-cell lines which undergo HIV-induced cell fusion are not appropriate model systems for the study of the loss of T4+ cells in HIV-induced AIDS.

THP.12 Murine Retrovirus Model Systems for Evaluating Antiviral Agents: Efficacy of AZT and ddC In vitro and In vivo.

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Two murine retroviral systems have been used to evaluate the efficacy of AZT and ddC. LP-BM5 MuLV induces a lymphoproliferative/immunosuppressive disease in adult C57BL/6 mice which has a number of similarities to human AIDS. Cas-Br-M MuLV induces a spongiform encephalopathy in NFS/N mice. In vitro studies have indicated that both AZT and ddC protect murine cells from infection with LP-BM5 and Cas-Br-M and inhibit the cell to cell spread of virus. ddC was effective at 50 to 100-fold higher concentrations than reported for human cells infected with HIV. Neither AZT nor ddC reduced virus release from murine cells chronically infected with MuLV. Preliminary experiments indicate ddC was ineffective in: (a) protecting C57Bl/6 from de novo infection with LP-BM5 (b) reducing virus load in infected mice (c) stimulating the immune response. In fact ddC appeared to depress the CTL response. AZT prevents the dissemination of Cas-Br-M MuLV and the development of neuronal degeneration in NFS/N when administered prior to or at the time of infection. Maternal transfer studies demonstrated that AZT-treated mothers transfer protective levels of AZT to their offspring. Newborn mice of AZT treated mothers challenged with 10^4PFU ic, had no detectible virus in their spleens or brains 3 and 8 weeks after AZT treatment. These results suggest that AZT treatment of an infected mother may inhibit viremia and protect newborns from MuLV infection.

THP.13 Phosphonoformic acid (Foscarnet) treatment and the effect on Human Immunodeficiency Virus (HIV) isolation

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Phosphonoformic acid (Foscarnet) is an efficient reverse transcriptase (RT) inhibitor in vitro and it has been shown to effectively inhibit HIV infection of H9 cells in tissue culture. The strong inhibitory effect on RT in addition to a low toxicity and little side effects make Foscarnet an attractive drug for treatment of HIV infected individuals. In the present study Foscarnet was given to 8 homosexual males with persistent generalized lymphadenopathy (PGL) or AIDS related complex (ARC) as a continous intravenous infusion at a dose of 0.14-0.16 mg/min/kg body weight/24 hours for 13-21 days. Virus isolations were initiated from peripheral blood mononuclear cells (PBMC) before treatment, the last day of treatment and at varying times after treatment. The results show that continous intravenous administration of Foscarnet reduced the frequency of positive HIV isolations from 13/14 (93%) before treatment to 18/34 (53%) after treatment. Foscarnet had no effect on the frequency of virus isolations in patients with advanced disease. PBMC cultures from these patients regularly yielded virus both before and after treatment. In contrast, PBMC cultures from patients with PGL were virus negative up to 8 weeks after treatment. No difference in sensitivity to Foscarnet was noted between different HIV isolates.

THP.14 Isolation of a novel type of human retrovirus from a healthy Swiss blood donor with faint HIV p24 antibody reaction by Western blot.

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Mass screening of blood donors by ELISA for HIV antibodies results in the detection of numerous individuals with repeatedly low-positive results. In at least half of these individuals, we detected faint antibodies reacting with gag proteins by Western blot. In order to investigate the origin of these antibodies, peripheral blood mononuclear cells of such individuals were routinely cultured and regularly tested for release of particulate reverse transcriptase activity. A novel type of infectious human retrovirus morphologically distinct from all animal or human retroviruses known so far was isolated twice from a healthy Swiss male blood donor with a slightly positive HIV ELISA and a faint p24 antibody reaction by Western blot. The person had credibly not been exposed to HIV and had no antibodies against other human retroviruses. The presentation will include up to date information on physical, biochemical, immunologic, and biologic properties of the virus as well as preliminary data on serology.

THP.15 HTLV-IV, LAV-2, SBL6669 and STLV-III Possess Transactivator Gene
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HTLV-III/LAV/HIV is the etiological agent of AIDS. It possesses a novel gene, termed tat, which is essential for its replication and as such but indirectly may play a role in its pathogenicity. Recently, new viruses antigenically related to HTLV-III and even more closely to STLV-III have been isolated from individuals from some West African countries. These include HTLV-IV, LAV-2 and SBL6669, isolated respectively from a lymphocytes of a healthy female prostitute, an AIDS patient, and an individual with lymphadenopathy. Some of these viruses cause immune deficiency whereas others may not. To test if the new viruses possess a tat gene, we linked their cloned 3'-LTRs to the bacteriological CAT gene. By DNA mediated transfection assays using virus-infected cells as the source of tat function and CAT gene as the test gene, we find that all three new viruses HTLV-IV, LAV-2 and SBL6669 as well as STLV-III possess a functional tat gene, irrespective of their pathogenic potential in vivo. Such structural and functional studies further suggest that (i) HTLV-IV, LAV-2 and STLV-III 3'-LTRs are structurally and functionally related, (ii) their transactivator genes are also structurally and/or functionally homologous, (iii) their 3'-LTRs and transactivator genes are related to HTLV-III LTR and transactivator gene and (iv) their LTRs and transactivator genes are more related among themselves than to HTLV-III.

THP.16 Antibody Reactions to Human B Cell Lymphotropic Virus(HBLV) in HIV Infection.
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We studied sera from patients with HIV infection for antibody to HBLV. Clarified, heat inactivated sera were reacted with phytohemagglutinin stimulated cord blood lymphocytes infected 4-5 days with HBLV (acetone fixed). Antibody was determined using fluorescene tagged goat antihuman antibody. Sera were screened for 3-4+ activity at a dilution of 1:40. 19/39 sera from patients with opportunistic infection (OI), 6/12 Kaposi's sera, 40/76 lymphadenopathy sera and 2/5 lymphoma sera were reactive with over 1/2 having titers of >1:160. In pts without HIV infection ,29/42 Hodgkins disease, 10/14 Acute lymphoblastic leukemia ,12/20 non Hodgkins lymphoma, 25/41 Crohn's disease,6/18 normal donors and 2/5 EBV negative sera reacted to HBLV often with titers greater than 1:160. Some 4+ sera showed reactivity to uninfected PHA stimulated CBLs and to nuclear antigen (ANA). Radio-immuno-precipitation antibody assay using 35[S] methionine labeled virus and uninfected control CBLs revealed that reactive sera produced 2 bands at 96-110,000mw and at 62-66,000mw. The disease produced by this virus and its role in HIV infection and other disorders still remains unclear. This virus is however widely distributed in man as are other better known herpes viruses.

THP.17 Human Immunodeficiency Virus (HIV) Encodes an Alternate gag Precursor Protein of 41 kDa.
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During actue HIV infection, two gag specific polypeptides of 55 and 41 kDa were shown to be rapidly labeled in an almost equimolar manner under pulse-chase conditions. Both of them were processed in an identical manner to mature gag polypeptides. p55 and p41 were readily expressed in a variety of non-lymphoid primate cell lines transfected with subgenomic proviral DNAs containing only the gag ORF under the control of HIV LTR, thus eliminating the possibility the p41 resulted from viral protease mediated processing of p55. p55 and p41 were metabolically labeled and purified from either persistently infected cells carrying a defective copy of proviral DNA or lymphocytes infected with virus prepared by transfection with cloned proviral DNA. Attempts at direct N-terminal sequencing of either protein failed, presumably due to blocked N-terminus. Comparative tryptic peptide mapping revealed that p41 peptide constituted a subset of p55. Four peptides unique to p55 were selected for automated N-terminal sequencing. Preliminary sequencing localized two such peptides to the N-terminal domain (residues 28-30 and 109-112) of the gag ORF. Although the exact N-terminus of p41 was not deduced, the wieght of the evidence suggested that p41 resulted from an alternate initiation at the MET codon at position 142 of the gag ORF. Functional role(s) of the p41 protein are being evaluated using mutagenized proviral DNAs incapable of expressing this protein.

THP.18 Comparison of 6 ELISA Assays for Detection of HIV antibody in African Sera
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African sera has been documented to cause many spurious results on ELISA assays because of immune complexes, auto-antibodies and many other immunologic reactions caused by continous exposure to endemic diseases. To systematically evaluate which tests are most effected by these conditions, we tested the Oreganon Teknika, Wellcome, Genetics Systems, Abbott, Electro-Nucleonics and Dupont ELISA assays on 300 well characterized patient sera collected at the Mama Yemo Hospital in Kinshasa, Zaire. Forty-four percent of the sera were HIV positive by western blot. The Oreganon Tecknika test was 99% sensitive and 98% specific in detecting HIV cases. The Wellcome test was 97% sensitive and 100% specific, the Genetics Systems assay 98% sensitive and 99% specific, The Dupont test 98% sensitive and 85% specific, the Abbott test was 100% sensitive and 72% specific and the Electo-Nucleonics test was 98% sensitive and 92% specific. The Wellcome test had the highest positive predictive value of 100%, Oreganon's was 98%, ENI's was 95%, Genetics Systems was 99%, Abbott's was 89% and Dupont's was 82%. Fifteen patients that were positive by the Dupont ELISA were asymptomatic, HIV antigen negative (Abbott), IgM negative (Dupont western blot) but p24 positive on IgG western blot. The results of the Dupont assay may represent either cross reactivity with other retrovirus infections or be false positive reactions. Almost all of the ELISA assays were able to detect true HIV infections however, in the African setting, the Wellcome test was the most rapid,(2 hours vs 4-6 for the others) and the easiest to use.

THP.19 Evaluation of a Latex Agglutination Assay Using Recombinant Envelope Polypeptides for Detection of Antibody to HIV
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Screening of blood donors for antibody to HIV is not feasible in most developing countries due to the lack of blood banking facilities and equipment, including refrigeration and ELISA readers. The cost of HIV ELISA kits and microplate ELISA readers is frequently prohibitive and technical support is often limited. Consequently, unscreened blood transfusions remain one of the major modes of HIV transmission in developing countries, such as in Central Africa where 5 to 15% of blood donors are seropositive to HIV. We therefore evaluated a rapid latex agglutination slide test for the detection of HIV antibodies in order to facilitate routine screening of blood transfusions in these areas. A recombinant HIV envelope antigen expressed in E. coli was attached to 0.5 microns latex beads, and mixed with 2.5 ul of patient sera diluted 1:10. Sera from 2,000 patients residing in Zaire, Kenya, Haiti, and Trinidad were evaluated by the latex agglutination slide test, ELISA (Organon-Teknika) and Western blot analysis (Dupont). Overall 64% of the sera were positive by repeat ELISA and Western blot. On a single determination for each sample the latex agglutination slide test was found to have a sensitivity of 99.1%, specificity of 99.4%, and positive predictive value of 99.5% compared to Western blot. The test was found to be simple, rapid (less than 2 minutes per test), and more specific than a single ELISA. Use of this assay will allow for the immediate implementation of blood bank screening for HIV in developing areas of the world where standard screening procedures are impractical or are not available.

THP.20 Humoral and Cellular Immune Response to Recombinant HIV Glycoprotein, gP120, in Rodents and Primates.
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A mammalian cell line has been developed that produces useful quantities of the major envelope glycoprotein, gP120, of Human Immunodeficiency Virus. The recombinant protein, r-gP120, is fully glycosylated and able to bind to CD4 (T4) antigen with high affinity. Rodents and primates immunized with r-gP120 incorporated in an adjuvant suitable for human usage (alum hydroxide) formed antibodies that reacted with native HIV glycoproteins gP160 and gP120 in Western Blot and radioimmunoprecipitation assays. Sera obtained from guinea pigs, rabbits, baboons, and chimpanzees contained antibodies that were able to neutralize viral infectivity in a variety of in vitro neutralization assays including: inhibition of reverse transcriptase, and VSV pseudotype assays. Chimpanzees immunized with r-gP120 developed a cellular immune response as measured by the ability of peripheral blood lymphocytes to proliferate in vitro in response to purified immunogen. Antibodies from several species were able to inhibit the binding r-gP120 to cell surface CD4 (T4) antigen in an in vitro binding assay. Finally, antibodies raised against r-gP120 from the HTLV IIIb isolate were able to neutralize, albeit at a somewhat lower titer, a number of diverse HIV-1 isolates including those obtained from Europe, Africa, and the United States. Sera from rodents and primates gave somewhat different patterns of cross neutralization, thus it appears that host factors may be important in determining the degree of protection that can be provided by a monovalent vaccine. These studies provide support for further consideration of r-gP120 as a vaccine against AIDS.

THP.21 Comparative Neuropathology of SIV and HIV Brain Infection.

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A strain of simian immunodeficiency virus (SIV/Delta, or STLV-III), originally isolated from a lymphoma from a rhesus monkey (Macaca mulatta), regularly produces immune deficiency and encephalitis when inoculated into juvenile rhesus monkeys. Brains from 5 infected monkeys were compared with those of 18 children who died with human immunodeficiency virus (HIV) infection and progressive encephalopahthy. A hallmark of the simian disorder is disseminated, multinucleated, syncytial cells occuring in liver, gastrointestinal tract, lymph nodes, spleen, and brain. Multinucleated giant cells in brain contain SIV particles on ultrastructural examination and are remarkably similar to those seen in the central nervous system of humans infected with the related retrovirus, HIV. In monkeys, these cells were predominantly perivascular, occurred in both gray and white matter and were often associated with foci of necrosis and karyorrhexis. Basal ganglia and deeper structures were frequently involved, as was the cerebral cortex; brainstem lesions were infrequent. In children with HIV encephalitis, such cells were often perivascular, but in some instances the cells bore no obvious relation to vessels. Diffuse white matter changes (pallor, astrocytosis) were only rarely observed with SIV but were common in children. One monkey had multinucleated cells in a leptomeningeal infiltrate. Complicating simian infections included simian cytomegalovirus and adenovirus. SIV infection in monkeys sufficiently mimics the human disease to warrant investigation of such pathogenetic features as penetration of virus into brain and syncytial cell formation.

THP.22 Identification of Functional Regions in the HIV Reverse Transcriptase by Site-Directed Mutagenesis

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We are currently studying the reverse transcriptase (RT) of HIV expressed in E.coli, with the aim of identifying those regions and specific amino acid residues involved in the catalytic activity of the enzyme. Initially, a large DNA fragment comprising most of the HIV pol gene, including the protease and RT sequences, was sub-cloned into an M13 expression vector which contains the strong inducible "tac" promoter. Infection of E.coli with this recombinant bacteriophage (mpRT1) resulted in significant levels of RT activity being induced. Through a series of manipulations, including oligonucleotide-directed deletion mutagenesis, the protease and endonuclease sequences flanking the RT coding region have been removed, giving a construct (mpRT4) which expresses large amounts of the native enzyme. The RT expressed by mpRT4 exhibits similar properties to the "authentic" enzyme found in HIV-infected cells, including sensitivity to PFA and AZT-TP, and apparent M_r (~66 kDa).

A number of regions of the RT which share homology with other polymerases have been probed by site-directed mutagenesis and using this approach, we have identified two small areas of the RT polypeptide which are likely to be involved in enzyme function, one of these being centred around two Asp residues (positions 185 and 186). It is hoped that studies of this nature will provide information about the interaction of HIV RT with its substrates and may facilitate the more rational design of chemotherapeutic agents.

THP.23 CELL SPECIFICITY OF HTLV-IV AND LAV-2 PROMOTERS

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Human T-lymphotropic viruses (HTLVs) display preferential spacificity for $CD4^+$ lymphocytes. This characteristic is partly due to the specificity of the virus-celluiar receptor interaction but could also be influenced by other celluiar factors and their interaction with viral promoters. We recently tested the ability of the HTLV-IV promoter to function in a variety of cell types. We linked the HTLV-IV 3'-LTR to the bacteriai CAT gene and measured the expression of the CAT gene to assess viral promoter function by DNA-mediated transfection assay. The HTLV-IV LTR-CAT DNA was transfected into human H9 and Jurkat lymphocytes, human HOS, rhabdomiosarcoma and gliai cells, and hamster CHO cells. The results showed that HTLV-IV promoter functions in all cell types tested and it appeared to function more efficiently in monkey COS cells. This suggests that the HTLV-IV LTR per se lacks tissue specificity in its function as a promoter. Similar observations have been reported previously for HTLV-I and HTLV-III.

THP.24 HIV-2 infection in a couple of french homosexual men.

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HIV-2 (Human Immunodeficiency Virus type 2) is a retrovirus isolated from AIDS patients from West Africa. Cross reactivity with HIV-1 is restricted to core proteins.

We have identified anti HIV-2 antibodies in two french homosexual men who never travelled to West Africa. One patient has AIDS (Kaposi's sarcoma) and the second, who is his sexual partner, is asymptomatic. In both cases, ELISA for anti HIV-1 antibodies was negative, Western blot only showed p 25 and p 34 in patient one, p 18 and p 25 in patient two. Those reactions, using HIV-2 antigens, were reactive ; Western blot demonstrated, in both patients, antibodies to p 26, p 16, p 55, gp 130-105, p 68, p 41, p 30-33. HIV-2 was isolated from the two patients peripheral blood lymphocytes.

Since Kaposi sarcoma was diagnosed in 1985 it could be speculated that HIV-2 infection occured in patient 1 at least two years before. This suggests that, now, HIV-2 infection could be spreading in homosexual french community. The negativity of the sera by HIV-1 ELISA has been already reported. Thus, in patients with AIDS or AIDS related complex, HIV-2 infection must be suspected when HIV-1 antibodies are lacking.

A blood-bank screening test using both HIV-1 and HIV-2 antigens is now required.

THP.25 Comparative Quantitative Investigations on HIV-1-neutralizing Antibodies with Respect to different Epitopes

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Quantitative determination of HIV-neutralizing antibodies is a prerequisite for developing vaccines. Using a sensitive plaque reduction assay 50 sera of HIV-1-infected patients showed a linear correlation between HIV-specific antibodies on the one hand and neutralizing antibodies on the other. Since all of the examined sera without exception showed this correlation one can conclude that in spite of the genetic variability of HIV-1 the majority of the neutralizing epitopes seems to be conserved. This indicates that similar as in Hepatitis B the total amount of (ELISA-determined) HIV-1-antibodies gives an information about the magnitude of the humoral immune status of the patient. - Further investigations concerning single epitopes on different structural proteins have been performed using synthetic oligopeptides. One neutralizing epitope located on p 18 showed a significant concentration-dependent correlation between ELISA-reactivity (based on an oligopeptide according to this epitope) and the neutralizing activity. Since 100 % of the patients sera (n=30) showed this behaviour one may conclude that this epitope has a high genetic stability. Similar results could be obtained with an epitope from gp 41 whereas another epitope on gp 41 showed no genetic stability. The capability of the epitopes to induce neutralizing antibodies was confirmed by an antiserum obtained from sheep immunized against the corresponding oligopeptide (the synthesis of the oligopeptide and the immunization was performed by Dr.Frenzel, Biochrom).

THP.26 Expression in E. coli, Purification, and Analysis of Full Length HIV gag Antigen

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The full length, non-fused HIV-IIIB gag gene product has been expressed at high level in E. coli. E. coli-expressed gag was obtained as a soluble protein and purified by cation exchange chromatography. Competition binding experiments indicate that all the immunoblot detectable gag-specific epitopes recognized by several AIDS patient sera are presented by full length E. coli-expressed gag. Thus, this protein will clearly be a sensitive reagent for the detection of gag-specific antibodies in human sera.

An high-titer antiserum specific for full length E. coli-expressed HIV gag was used to detect gag-derived proteins by Western blot in a licensed preparation of purified virus. In addition to p55, p24, and p17, minor gag-derived proteins were detected at approximately 130 and 41 kDa. We note that this gag-specific reactivity in a Western blot could be falsely interpreted as HIV env reactivity (gp160/120 and gp41). In addition, HIV gag-specific antisera are being used to examine cross-immunoreactivity between gag proteins from different viruses.

THP.27 HIV tat/LTR-mediated Expression of Heterologous Genes: Derivation of Stable Cell Lines

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Stable cell lines carrying a functional HIV tat gene, a reporter gene linked to the HIV LTR, or combinations of these genes, have been isolated following DNA co-transfection of appropriate plasmid constructions and pSV2-neo as a selectable marker into HeLa cells. Clones constitutively expressing a functional tat gene product (under SV40 early transcriptional control) were identified by the ability of such clones to express a high level of chloramphenicol acetyl transferase (CAT) shortly after transfection with a HIV LTR-CAT plasmid. Clones carrying HIV LTR-CAT or HIV LTR-β-galactosidase plasmids in an activatable form express low or undetectable levels of the reporter gene protein, but are readily activated to high level expression by the introduction of a HIV tat-expressing plasmid. Clones expressing high levels of β-galactosidase under combined HIV tat/LTR control have been isolated, but no stable lines expressing high levels of CAT activity under HIV tat/LTR control could be derived. This observation suggests that high level expression of the CAT gene product is lethal for HeLa cells. Similar experiments using human IL-2 as a reporter gene are in progress. Our results demonstrate the derivation of stable cell lines containing heterologous genes under tight HIV tat/LTR control. Such cell lines should be useful for further studies of the mechanism of tat function, and for high level expression of heterologous genes in HeLa cells.

THP.28 Rapid Direct Detection of HIV in Lymphocytes of Seropositive, Asymptomatic Persons by Selective DNA Amplification.

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Confirmation of current infection with HIV requires virus isolation by cocultivation of patients' lymphocytes with PHA-stimulated lymphocytes from normal individuals. This requires up to 3 weeks with virus only being isolated from a portion of seropositive individuals. We have used a modified form of a DNA amplification technique to rapidly detect HIV sequences in chromosomal DNA isolated directly from patients' lymphocytes without prior cultivation. Two oligomer primers of 20 nucleotides each and an oligomer probe of 40 nucleotides from the highly conserved amino terminus of gp41 were used. HIV sequences from patients' lymphocyte DNA were amplified using DNA polymerase I in the presence of the two primers to give rise to a 135 bp partial gp41 sequence. Amplified HIV sequences were hybridized with a 32-P end-labeled 40-mer probe representing a portion of the 135 bp sequence. This was followed by digestion with Hha-I yielding a diagnostic end-labeled 24-mer. We analyzed DNA isolated from established HIV-infected T cell lines, uninfected T cells, T cells infected in vitro with HIV, and DNA isolated directly from lymphocytes of sero- and culture-positive asymptomatic gay males from San Francisco. We could readily detect, within 2 days, the 24-mer in 8 of 12 gay males tested and in all of the infected T cells but not in any of the uninfected T cells. This technique enables us to readily identify HIV-infected persons directly. We will present additional data on the HIV status from a large number of persons who are: 1) asymptomatic seropositive long term survivors; 2) sero-positive but culture-negative persons; 3) sero-negative spouses of sero-positive persons; and 4) offspring of sero-positive mothers.

THP.29 Serological comparison of human retroviruses of West African origin.

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Among sera tested in our laboratory for antibodies to human immunodeficiency virus (HIV) we found three anti-HIV ELISA positive sera from West African immigrants which by Western blot (WB) and radioimmunoprecipitation (RIP) analyses reacted with gag and pol gene encoded proteins (p 24, 31, 53-55, 64) but not with envelope glycoproteins (gp 41 and 120) of HIV. However, these sera reacted with envelope as well as core proteins of the West African retroviruses human T lymphotropic virus type IV (HTLV-IV) and lymphadenopathy associated virus type II (LAV-II). A retrovirus (SBL-6669) was isolated from lymphocytes of one the West African individuals, a 55-year old Gambian woman who had a decreased number of T4 cells, recurrent lower respiratory tract infections and ungal candidiasis. Comparison of this virus with HTLV-IV, LAV-II and HTLV-IIIB by WB and RIP analysis showed that SBL-6669 virus was antigenically more closely related to HTLV-IV and LAV-II than to HTLV-IIIB. The external glycoproteins of the three West African viruses SBL-6669, HTLV-IV and LAV were indistinguishable However there were interstrain differences in the size of core proteins and the presumed transmembrane glycoproteins. SBL-6669 virus was associated with immunodeficiency like LAV-II (Clavel et al, Science 1986; 233: 343) but unlike HTLV-IV (Kanki et al, Science 1986; 232: 238).

THP.30 Immunoperoxidase Localization of Human and Simian Immunodeficiency Antigens in Surgical Pathology and Autopsy Specimens.

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Surgical lymph nodes from 23 AIDS patients, fixed in B-5, and selected autopsy specimens from 39 AIDS cases, fixed in formalin, were stained by the ABC immunocytochemical technique using polyclonal and monoclonal antisera to localize HIV (also known as HTLV-III/LAV) antigens including core protein p24. Biopsy specimens with follicular hyperplasia had immunoreactive viral antigens in follicular dendritic cells, rare immature B lymphocytes and extracellular spaces of follicles, sinus macrophages and postcapillary venule endothelium, while atrophied nodes were usually not immunoreactive. In 2/8 cases of Kaposi's sarcoma, histiocytic cells or vascular endothelium was immunostained in lymph nodes with metastatic tumors. A small proportion of multinucleated giant cells and mononuclear macrophages were immunoreactive in 8 of 15 brains with such cellular infiltrates including 3 cases of Progressive Multifocal Leukoencephalopathy and in vascular endothelium of one case. Monkeys, Macaca mulatta or Macaca fascicularis, inoculated with Simian Immunodeficiency Viruses (SIV III/Delta or MnIV [WPRC-1]) had viral antigens in macrophages, reticular cells and giant cells in sections of formalin fixed tissues with lymph node follicular hyperplasia, lymph node and splenic giant cell histiocytosis, and in retroviral encephalitis.

THP.31 The Acquisition of Anti-HIV Markers during Seroconversion observed in 40 High Risk Males.

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A retrospective serological study was performed on 340 sera obtained from 39 homosexual/bisexual men and one haemophiliac male during seroconverion after infection with Human Immunodeficiency Virus (HIV). The serial bleeds from each patient were collected at random intervals over 4 years. Follow up periods from the time of seroconversion range from 3 months to 3.5 years. Tests performed on the specimens include enzyme linked immunosorbent assay (ELISA), radioimmunoprecipitation (RIP) test for anti-p24 and western blotting (WB).

A 'window period' (ranging from 2 weeks to 5 months) of low sensitivity with the ELISA as compared with the WB was observed in early specimens from six patients. The earliest reactivity detected by WB was to core proteins p24, p40 and p55 followed closely by reactivity to viral enzymes (p34, p53/p68) and glycoproteins (gp41-45, gp110). The RIP test was the least sensitive assay. Five patients were consistently RIP negative for all specimens, two of whom developed AIDS.

These results support recent observations concerning the poor sensitivity of available ELISA's in early HIV infection during which time the WB assay detects anti-HIV core antigen reactivity.

THP.32 Live Vaccinia/HIV recombinant Viruses. An approach to an AIDS Vaccine

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Both HIV lentiviruses and HIV-infected cells are presumed to present a single major target antigen at their surfaces. This polypeptide, the env glycoprotein, is thought to promote HIV infection by interaction with a host protein, possibly the lymphocyte T4 antigen. The 160 kilodalton env precursor glycoprotein (gp160) undergoes proteolytic cleavage in vivo, yielding a gp41 transmembrane moiety and a gp120 extracellular component. By analogy to the gp's of similar viruses, these have been presumed to remain associated at the cell surface. We have expressed the HIV env gp160 precursor glycoprotein gene in a recombinant vaccinia virus. env glycoprotein encoded by the recombinant virus VVTGeLAV is correctly cleaved to generate gp41 and gp120. However, the two moieties do not remain associated, gp120 being rapidly shed from the cell surface. We have constructed mutants of VVTGeLAV in which the env cleavage site(s) has been removed, and the immunological properties of these second-generation recombinants will be discussed.

THP.33 LAV-2/HIV-2 infection : Clinical, epidemiological and virological features
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In 1986 we diagnosed 18 cases of LAV-2/HIV-2 infection in patients (pts) who have been living in France for at least one year. Six pts were assumed to have AIDS whose 2 met the criteria for AIDS since 1983. Two pts presented with ARC diagnosed in 1985. Ten were asymptomatic subjects (AS). Eleven pts originated from West African countries : Cape Verde islands (2), Ghana (3), Ivory Coast (1), Guinea (2), Senegal (2) and Guinea Bissau (1). Seven pts were european : 2 heterosexual Portuguese couples, one French heterosexual male and a French couple of homosexual males.

In these pts, HIV-2 transmission was likely to be acquired through heterosexual or homosexual contacts. None was a drug abuser. In the 2 heterosexual Portuguese couples, the mode of HIV-2 transmission is quite unclear. Vertical transmission is studying in 3 cases of HIV-2 pregnant women. Retrovirus isolation was performed from the peripheral blood lymphocytes from the 12 tested patients (5 AIDS, 2 ARC, 2 AS). In the supernatants of the cultures, an antigen capture assay using HIV-1 polyclonal antibody did not detect HIV-2 antigens. Isolates were characterized by Dot Blot hybridization with HIV-1 and HIV-2 DNA probes. We are performing Southern Blot analysis of isolates from patients originating from different countries. HIV-2 neurotropism was demonstrated by virus isolation from the CSF and/or by intrathecal IgG HIV-2 synthesis. IgG antibodies to HIV-2 were detected by Elisa and WB (Diagnostics Pasteur). Since the HIV-1 and HIV-2 cross-reactivity was restricted to the core proteins, only the presence of antibodies to HIV-2 envelope glycoproteins demonstrated HIV-2 seropositivity. Whatever HIV-1 and HIV-2 common characteristics, as lymphotropism and cytopathic effect in vitro, question is asked about a difference of pathogenicity.

THP.34 Evaluation of Microinjection of Cloned Genes as an Effective Method of Genetically Engineering Mammalian Cells to Produce Human Immunodeficiency Virus and Envelope Protein
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A cloned HIV, strain HTLV-IIIB (pHXB-2), infectious provirus was microinjected into the cell nucleus of six non-lymphoid cell lines from caprine, ovine, bovine, and human species. For each cell line, 100-200 cells were microinjected with pHXB-2. An immunofluorescence assay (IFA) for HIV p24 demonstrated virus replication 24-48 hrs after microinjection in 5% of the cells. Virus was recovered from all cell lines regardless of tissue or species of origin by cocultivating T4-positive human lymphocytes (H-9) with the microinjected cells 48 hrs after microinjection. Confirmation of infectious virus release from injected cells was demonstrated by syncytia formation, electron microscopy, reverse transcriptase, and radioimmunoassay for HIV p24 in cocultures. Syncytia in cocultivated H-9 cells were apparent on days 7-10 and was both the earliest indicator and most reliable assay for demonstration of infectious virus release. A complete envelope subgenomic fragment of pHXB-2 flanked by 5' and 3' LTRs (pLVWT) was constructed and introduced into mammalian cells in an attempt to create a cell line expressing high levels of the HIV envelope free of infectious virus. Using an antiserum to gp120, the major outer envelope protein of HIV, 5-20% of the microinjected cells were found to express low levels of envelope proteins by IFA. No replicating virus was detected and the duration of expression has not yet been determined. These results suggest a possible approach to producing antigens in mammalian cells and may have relevance for vaccine development.

THP.35 HIV Neutralizing Antibodies and Cellular Immunity Elicited by a Recombinant Virus Envelope Produced in Insect Cells
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The HIV envelope (gp160) was produced in insect cells using a baculovirus expression vector encoding the HTLV-III_B envelope. Antibodies from animals immunized with this protein neutralize the HTLV-III_B virus and the neutralization titer of this antisera is approximately five-fold higher than that of antisera to native gp120 isolated from the virus. The neutralization of the gp160 antisera is type specific in that it does not efficiently neutralize the heterologous variants, HTLV-III_{MN} and HTLV-III_{RF}. In addition to eliciting a humoral immune response, gp160 elicits cellular immunity as measured by T-cell proliferation upon stimulation by virion or native gp120. In contrast to the humoral response, cellular immunity is not HIV isolate specific. We are preparing the envelope from other viral variants to obtain a more broadly neutralizing response and to evaluate these proteins as a vaccine.

THP.36 Isolation and Characterization of a Bacterially Expressed Reverse Transcription of HTLV III/LAV
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Various fragments of the "pol" region of HTLV III/LAV were cloned into different expression vectors. Enzymatically active reverse transcriptase was detected with two of them in transformed bacteria. Furthermore, two protein bands of 66 and 51 kD were detected in bacterial lysates using patient sera suggesting that they represent the reverse transcriptase subunits β and α. Processing from larger molecules, which presumably represent precursor forms, could be followed with time. The enzyme activity was purified by means of DEAE-Sephadex, phosphocellulose, mono S and immuneaffinity column chromatography. Biochemical parameters of the bacterial polymerase were compared with virion-associated reverse transcriptase. Inhibitor studies as well as fidelity studies were performed and will be presented. The enzyme should be useful for large scale screening of reverse transcriptase inhibitors.

THP.37 Inactivation of HIV by Disinfectants and Spermicides
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Various disinfectants and spermicides have been tested for their efficacy to inactivate in vitro the reverse transcriptase and the infectivity of HIV for human peripheral blood lymphocytes. Disinfectants commonly used in hospitals for cleaning floors and benches were containing alcohol in quaternary ammonium or aldehyde complex solutions or glutaraldehyde in quaternary ammonium solutions. All these solutions were found to be effective either undiluted or at concentrations ranged between 0.25 % and 25 % with a time of treatment varying from 1 to 10 min. at room temperature. Disinfectants for medical instruments were mainly aldehyde solutions and were also destroying viral activities. Commercialized solutions for body hygiene are often a mixture of alcohols with other compounds such as quaternary ammonium salts or chlorohexidine for example. Five of them were tested and found effective at various concentrations (0.5 % to 50 %) in a short time of contact with the virus (30 sec. to 5 min.). Inactivation of HIV by spermicides containing cationic detergent (benzalkonium chloride or alkylbenzyldimethyl ammonium chloride) has also been shown to inactivate HIV infectivity in vitro at low concentrations in a relatively short period of treatment (10 to 60 min.). The effects of other spermicides and disinfectants will also be discussed. These results might be of interest for the prevention of the sexual transmission of the disease and for the safety in hospitals and laboratories.

THP.38 A MONOCLONAL ANTIBODY TO GENETICALLY ENGINEERED NON-GLYCOSYLATED GP120 PRODUCED IN YEAST NEUTRALIZES HIV.
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A murine monoclonal antibody specific for a genetically engineered polypeptide produced in yeast corresponding to amino acids 28-491 of the envelope gene product of the ARV-2 isolate (now designated HIV-SF2) of human immunodeficiency virus (HIV), is able to neutralize the infectivity of HIV-SF2 in vitro. This monoclonal antibody, referred to as 95C9, reacts with glycosylated HIV-SF2 gp120 in immunoblot assays. In addition, it also reacts specifically in immunofluorescence assays with acetone-fixed HIV-SF2-infected cells. By using recombinant HIV-SF2 antigens corresponding to subregions of gp120, 95C9 was shown to react with an epitope between amino acids 28 and 277 of the HIV-SF2 env gene product. Assays with other HIV isolates, showed that 95C9 was reacting with an epitope that was not conserved among all HIV isolates; 95C9 did not react in either immunoblot or immunofluorescence assays with HIV-Zr6 or LAV-BRU, two virus strains which show considerable divergence from HIV-SF2 in their gp120 coding regions. Neutralization assays with these two isolates, and other HIV strains, are in progress. In addition we are attempting to map the precise location of the 95C9 reactive epitope.

THP.39 Stability of RNA stem-loop Structure and Distribution of Non-Random Structure in Human T-cell Lymphotropic Virus Type III

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The stability of predicted RNA stem-loop structure in human T-cell lymphotropic virus type III has been tested statistically using a Monte Carlo simulation method. The distribution of statistically significant stem-loop structure have been obtained. We can find the characteristic patterns in the 5' non-coding region, boundary region between the protein coding frames and 3' non-coding region. Especially, the size of the distinct and significant secondary structure occurring in the 5' terminal region has been assessed under different window sizes using Monte Carlo method above. The predicted secondary structure with about 100 nucleotides is preferable to those with other size in 5' non-coding region. Moreover the distributions of significant stem-loop structures in the 5' terminal of ARV-2, LAV and H9/HTLV-III have also been computed. The possible correlations between the AIDS virus genome biological function with the predicted non-random, significant stem-loop structures are discussed. Our results support recent experiment results, in which the possible stem-loop structure of the 5' region of HTLV-III mRNA is involved in translational control.

THP.40 Tests for Virus Yield Control in HIV Infected Cell Culture During Preparation of Teat-System for AIDS Serodiagnostics.

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Conventional variant of immuno-enzyme test-system based on purified and concentrated HIV antigen has been developed. To obtain the antigen, HIV strain IVA 85 isolated at the Ivanovsky Institute of Virology in 1985 and adapted to continious lymphoid cell line has been used. During productivity control of chronically infected IVA 85 culture for cell fraction control, electron microscopy, indirect immunofluorescence, and immuno-enzyme assay with cell suspension adsorbed on plates or their lysates in various concentrations were applied. HIV antigen in liquid fraction was determined by

i EIA-capture with human IgG to HIV adsorbed on plates and with the same antibodies labeled by horse-radish peroxidase,

ii indirect EIA with the adsorbed on the plates dilutions of 100-fold concentrates of cultural fluid.

Along with that, rate of virus accumulation in the cells in cultural fluid was evaluated by hybridization with molecular probe.

Complex of the methods used gave possibility to choose an optimal passage scheme. Until now, IVA 85 culture passed 70 consequent passages without fresh lymphoid cells addition with 70-85% of antigen-containing cells. Data of examination of 600 sera prove system specificity to be 99.6-100%.

THP.41 Bacterial Pneumonia and HIV Infection in Parenteral Drug Users without AIDS

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Epidemiologic data from New York City (NYC) demonstrate a sharp increase in non-AIDS pneumonia deaths among intravenous drug abusers (IVDAs) since 1981. We studied the incidence of bacterial pneumonia in a well-defined population of IVDAs without AIDS, and examined the association with HIV antibody (Ab). All hospitalizations over a 12 month period were monitored among 436 IVDAs in a NYC methadone program (MMTP) enrolled in a prospective study of HIV infection. Hospitalizations were identified through active surveillance by MMTP staff. Both MMTP and hospital staff were blinded to patients' HIV Ab status. Hospital charts were reviewed for all pneumonia cases. Pneumonia was defined by infiltrate on chest x-ray; organisms were identified by Gram stain, blood and/or sputum culture, or serology.

Surveillance began 10/1/85. At entry, there were 159 seropositives (SPs) and 277 seronegatives (SNs). By 9/30/86, 115/159 (72%) SPs and 236/277 (85%) SNs remained in the MMTP ($p<.05$). Over 12 months, 14/159 (9%) SPs vs. 6/277 (2%) SNs were hospitalized for bacterial pneumonia; odds ratio (O.R.)=4.4 (C.I. 1.6 - 11.6, $p<0.005$). In the SP group organisms were Hemophilus influenzae (6), Streptococcus pneumoniae (5), Staphylococcus aureus (1), Escherichia coli (1), and Legionella pneumophila (1). In the SN group, organisms were H. influenzae (4), S. pneumoniae (1) and Klebsiella pneumoniae (1). Two cases in SPs were fatal vs. none in SNs. Pneumonia was more highly associated with HIV Ab in patients reporting no current IV drug use: for those not using drugs at study entry, O.R.=6.7; for those still using, O.R.=2.0.

These results indicate a remarkably high incidence of bacterial pneumonia among SP IVDAs without AIDS (minimum yearly rate = 88/1000), with a case-fatality rate of 2/14 (14%). Association with HIV Ab was not attributable to increased drug use among SPs. The high frequency of infection with S. pneumoniae and H. influenzae suggest the need for study of immunization of SP IVDAs against these pathogens.

THP.42 Human Immunodeficiency Virus Viremia in Homosexual Men with Lymphadenopathy

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Seventy-five homosexual men with lymphadenopathy syndrome (LAS), defined as lymphadenopathy in 2 or more extrainguinal sites for $\geq$3 months, were enrolled in a prospective study in Atlanta in 1982-1983. All were seropositive for antibody against human immunodeficiency virus (HIV). As of January 1987, 16 (21%) of these men have developed the acquired immunodeficiency syndrome (AIDS). Cultures for HIV were performed on lymphocytes from 109 peripheral blood specimens from 66 of the 75 study participants, including 12 who subsequently developed AIDS. Cultures were screened for up to 4 weeks for reverse transcriptase (RT) activity. Of 23 men with positive results (defined as $\geq$10000 RT counts/0.4 ml) on the first sample, 15 were cultured a second time; all but 2 remained positive. Of 43 men with negative results on the first sample, 12 were cultured again up to 36 months after the first sample was obtained. Three were positive on the second sample and 3 others on the fourth; 6 have remained culture negative in up to 5 specimens. Men who were initially culture positive and men who were culture positive on any occasion were more likely to progress to AIDS than culture negative men (9/23 vs. 3/43, p=.002; 10/29 vs. 2/37, p=.003; respectively). Culture positivity is a marker for progression to AIDS and is likely to develop in most men with LAS. The confidence that there exists a subgroup of men that remain culture-negative and have a better prognosis is diminishing with time.

THP.43 Frequency of Clinical and Laboratory Abnormalities among HIV Antibody Seropositive and Seronegative Gay Men.

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We report frequency of clinical and laboratory abnormalities among subjects seropositive and seronegative for HIV antibody in a prospective study of three groups of gay men in San Francisco: an STD clinic group, a randomly selected neighborhood group, and sexual partners of men with AIDS. Of 320 subjects seen at one-year followup, 64% (205/320) were seropositive for HIV antibody by ELISA with Western Blot confirmation. Oral candidiasis and oral hairy leukoplakia were clinical findings observed only in seropositives, 9% and 3% of seropositives, respectively. Three laboratory measures were seen only in seropositives: platelet count $\leq$ 120,000 (9% of seropositives), ESR $\geq$ 22 (9%), and H/S ratio $\leq$ 0.6 (35%). Generalized lymphadenopathy was found in 55% of seropositives and 12% of seronegatives. Frequency of other measures in seropositives and seronegatives, respectively, are as follows: shingles, 10% and 5%; hemoglobin $\leq$ 14.2, 23% and 3; WBC $<$ 4.6, 37% and 9%; lymphocytes $\leq$ 1500, 21% and 7%; and absolute T-helper count $\leq$ 400, 32% and 3%. H/S $<$ 1.0 was found in 55% of seropositives and 15% of seronegatives, whereas H/S $\leq$ 1.5 was found in 72% of seropositives and 71% of seronegatives. A significantly higher percent of seropositives in the STD and partner groups had an H/S ratio $<$1.0 (61% and 58%) than in the randomly selected group (38%) (p=0.008), indicating possible greater duration of infection in those groups or cofactor effects or both.

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THP.44 HIV Seroprevalence Among Connecticut Intravenous Drug Users in 1986.

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The rising seroprevalence of HIV infection among Connecticut intravenous drug users (IVDU) in 1986 was monitored by anonymously testing all admissions to selected drug treatment programs for HIV antibody. The largest number of sera (171) were obtained from entrants to the New Haven Substance Abuse Treatment Unit. In 1986, 22.2% (38/171) of those seeking treatment for active intravenous drug use were Western blot (WB) confirmed HIV seropositive. Interview questionaire data on 114 of these entrants have been analyzed. Significantly more of the blacks (81.8%-18/22) and of the Hispanics (40%-2/5) than of the whites (10.4%-9/86) were WB seropositive ($p<0.0001$, chi-square) among this 76% white group. Seropositives were older (mean-33 vs. 30 years, $p<0.007$, t-test) and had a longer history of drug injection (mean-14.3 vs. 10.6 years, p=0.03, t-test). There was a non-significant trend toward more needle uses in the past year among seropositives. Sixty-eight percent (76/112) had shared needles in the past year. There was no association between sharing and seropositivity or between sharing and race. Most attempted to clean shared needles.

HIV seroprevalence and interview data were assessed in an additional 147 entrants to methadone programs in 3 other Connecticut metropolitan areas. For entrants to all program locations, including 114 from New Haven, seroprevalence decreased with increasing distance from New York City ($p<0.01$, Mantel test for trend). Stratified analysis, controlling for program location, showed that blacks (odds ratio-15.0, 95% confidence interval (CI)-7.1-33.0) and Hispanics (odds ratio-8.8, 95% CI-2.6-30.4) were significantly more likely to be seropositive than whites ($p<10^{-6}$ and $p<0.01$, respectively, Mantel-Haenszel chi-square).

THP.45 Cause-Specific Mortality Rates for the Acquired Immune Deficiency Syndrome (AIDS) Dade County, Florida 1985.
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Dade County, Florida, which encompasses the greater Miami metropolitan area, is situated in the lower southeastern portion of the State of Florida. As of January 23, 1987, 869 cases of AIDS, with Dade County morbidity, had been reported to the AIDS Program, State Health Office, Department of Health and Rehabilitative Services, Tallahassee, Florida.

To assess the impact of this disease for 1985 in Dade County, deaths attributable to AIDS were identified. The Florida AIDS case registry, death certificates, and medical examiner logs were reviewed and 145 of the 17,324 total 1985 Dade County deaths (0.83) were classified as AIDS deaths.

Dade County 1985 midyear population estimates (white 1,305,282; non-white 461,670) were used to establish crude cause/race-specific mortality rates. The crude AIDS cause specific mortality rate for Dade County was 8.2 deaths per 100,000 population. AIDS mortality by race consisted of 77 non-white and 68 white deaths. Population adjusted data developed a 3.2:1 non-white/white ratio. There was a statistically significant difference between non-white/white deaths 16.7/5.2 per 100,000. ($p<.05$).

These mortality rates were compared to other leading causes of death in Dade County. AIDS non-white deaths exceeded deaths due to motor vehicle accidents (16.7/13.4 per 100,000) and approached white homicide deaths (18.9 per 100,000) for Dade County 1985.

THP.46 Prevalence of Human Immunodeficiency Virus (HIV) Infection in Ethnic Minority Homosexual/Bisexual Men.
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Of 1034 participants in a randomly selected prospective cohort of single men between the ages of 25 and 54, 816 (78.9%) are homo/bisexual and of these 100 belong to ethnic minorities. We examined four minority groups and the only significant differences in prevalence or incidence of infection were between black and white men. We observed a higher proportion of HIV infection among blacks, 19 of 29 (65.5%) than among whites, 341 of 700 (48.7%). Blacks also experienced a higher rate of HIV seroconversion than whites during the 24 months of follow-up; among the 10 HIV seronegative blacks who entered the study, two (20%) became infected while among 359 seronegative whites, 23 (6.4%) became infected.

To explain these findings, three established risk factors for the transmission of HIV infection--needle sharing, multiple sexual partners and frequent receptive anal/genital contact--were examined. Whereas a slightly higher proportion of whites shared needles and had multiple sexual partners than blacks and a slightly higher proportion of blacks had frequent receptive anal/genital contact than whites, none of the differences were significant. Available measures of socio-economic status also did not differ by race. Other reports have indicated that blacks are disproportionately represented among AIDS cases nationally, and they have suggested that the findings are due to increased prevalence of IV drug use. Here, needle use does not explain the difference; our findings suggest the need for further investigation into the role of race and HIV infection.

THP.47 Risk Factors for Seroconversion with Human Immunodefiency Virus Among Homosexual Men in San Francisco, 1983-1987.
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Two prospective studies in San Francisco have identified 37 homosexual or bisexual men who developed serum antibodies to human immunodeficiency virus (HIV) during study surveillance, 1983-1987. In the year prior to acquisition of HIV antibody, 74% of seroconverters reported receptive anal intercourse, 77% reported insertive anal intercourse and 100% receptive oral intercourse. Sixty-eight percent reported using drugs during sexual activity.

When compared to HIV seronegative controls, men who acquired antibody had a greater number of male intercourse partners ($p<.0001$), and were more likely to have reported: receptive anal intercourse ($p=.009$), receptive oral intercourse ($p=0.04$) and use of either cocaine, amphetamines, depressants, or hallucinogens during sexual activity ($p=.0005$). When entered into logistic analysis with number of sexual partners and specific sexual practices, use of the above drugs was significantly associated with antibody to HIV (odds ratio 3.29, $p=0.01$).

Of nine men who denied receptive anal intercourse in the year prior to HIV infection, seven reported insertive anal intercourse. The two men who denied both practices recalled receptive anal intercourse in the preceding 18 months. Eight of these nine men acquired antibody late in the studies.

The proportion of men who acquire HIV infection through receptive anal intercourse may be decreasing, and less efficient modes of transmission may become more apparent. Use of drugs during sexual activity may contribute to risk of HIV infection.

THP.48 Male-to-Female Transmission of Human Immunodeficiency Virus (HIV): Current Results, Infectivity Rates, and San Francisco Population Seroprevalence Estimates.
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Eighty-nine female partners of men who were infected with HIV or diagnosed with AIDS or ARC have been interviewed and tested. More than 50% were the partners of bisexual men. Overall, 20% of the women were infected (95% confidence interval: 13%-30%). Based on the reported number of sexual contacts with the infected partner, we were able to calculate a per exposure infectivity rate of .001 (95% confidence interval: 0-.0024). However, the infectivity rate was almost 1.8 times higher for women who practiced anal intercourse than for those who practiced only vaginal and oral sex. This higher rate is comparable to the anal-receptive infectivity rates reported for male-to-male exposure.

Using these estimated infectivity rates in conjunction with survey data on the number of male partners of heterosexually active women in San Francisco, combined with estimates of seroprevalence in their male partners, we project that approximately 4 of 1000 such women may have been infected by these men. We conclude that penile-vaginal contact, a well documented risk, is a less efficient means of transmission than is penile-anal intercourse. Higher rates of heterosexual transmission reported elsewhere are probably attributable to factors such as greater numbers of exposures (sexual contact with an infected partner), parenteral exposures, or to other co-factors and behaviors not prevalent in this sample.

THP.49 Natural History of HIV Infection in a Cohort of Homosexual Men from Los Angeles.
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63 patients with biopsy-proven persistent, generalized lymphadenopathy (PGL), and 67 asymptomatic gay control men were evaluated every six months with serial repeat node biopsies, HIV and EBV serology and virology, and immunologic function. Median follow-up interval is 1.3 yrs (0-53 mos). Mean age of pts was 32.4 yrs, vs. 34.7 yrs in controls. In the PGL cases, 73% were white, 13% black, and 15% Hispanic. At study entry, 62/63 (98%) PGL cases were HIV seropositive, vs. 36/66 (55%) of gay controls ($p<.05$). With follow-up, 2 additional controls have become HIV positive and all PGL cases are HIV positive. Rates of conversion are as follows:

Conversion from HIV- to HIV + Control=7.1%/person-year
Conversion from HIV + control to any ARC=17.3%/person-year
Conversion from HIV + control to PGL=7.4%/person-year
Conversion from PGL to any AIDS condition=9.2%/person-year
Conversion from PGL to lymphoma=3.9%/person-year

Two variables were significantly ($p=.01$) associated with increased risk of conversion from PGL to lymphoma: increased gamma globulin fraction, and increased IgG level at PGL diagnosis. Three variables significantly associated with increased risk for conversion from PGL to AIDS were (1) decreased T4, (2) decreased T4/T8 and (3) increased IgA, at time of PGL diagnosis.

THP.50 Laboratory and Clinical Manifestations of HIV Infection in Patients with Congenital Clotting Disorders (CCD).
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The Transfusion Safety Study is a multicenter cooperative evaluation of factors influencing risk of transfusion-transmitted HIV infection and progression. TSS has clinical and laboratory data on 456 treated CCD patients (426 male, 20 female), of whom 58% are anti-HIV(+). We recorded clinical signs (unexplained weight loss or diarrhea, generalized lymphadenopathy, thrush or zoster) and laboratory findings (platelets < 100K, lymphocytes < 1000 or T4 lymphs < 200).

A higher percentage of anti-HIV(+) patients (19% vs 2%, $P<.001$) had one or more abnormal findings. Three patients had AIDS. Lymphadenopathy was the only clinical sign significantly more frequent in anti-HIV(+) patients ($P=.007$). Among laboratory findings both lymphopenia and low T4 counts were more frequent in anti-HIV(+) patients ($p<.001$). Anti-HIV(+) patients were likelier to have lymphopenia if 15+ years and low T4 counts if 35+ years. The likelihood of manifestations in anti-HIV(+) patients did not appear to depend on type of treatment (factor 8 or 9 concentrates or single donor components). These data show that, thus far, most anti-HIV(+) CCD patients are clinically well though they may have laboratory manifestations of HIV infection. (Supported by Contract No. NO1-HB-4-7003 of the National Heart, Lung and Blood Institute.)

THP.51 PREVALENCE OF HIV ANTIBODIES AMONG INTRAVENOUS DRUG USERS IN LOS ANGELES

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Although Los Angeles County has the third largest number of AIDS cases nationwide, the percent of AIDS cases who are intravenous drug users is low (11%) compared to the East Coast rate of approximately 70%. To assess the prevalence of HIV antibodies in our intravenous drug addict population a random sample of 728 individuals, enrolled in either methadone maintenance or detoxification programs, were interviewed between April and July 1986.

Detailed demographic data, medical, sexual and drug use histories were obtained, and blood was drawn for determination of HIV antibody status, markers for hepatitis B, and VDRL. Only 13 (2%) participants were seropositive. Sixty-nine percent of the positives were white compared to 55% of the negatives; 23% were hispanic compared to 34% of the negatives; the percentage of Blacks in both groups was the same. Seven of the HIV antibody positives were male, of whom 5 were homosexual or bisexual. Of the 6 positive females, 3 admitted to prostitution. Although the seroprevalence is extremely low, 92% of the seropositives and 96% of the seronegatives admitted to sharing needles. Therefore, timely education efforts must be targeted to modify these high risk behaviors before the prevalence rate rises precipitously.

THP.52 Screening of U.S. Populations for the Presence of LAV-II

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A new human retrovirus was isolated from people in West Africa and Europe by scientists at the Pasteur Institute, Paris, France. The virus, designated as LAV II, appears to be transmitted in a manner similar to Human Immunodeficiency Virus (HIV) and cause similar symptoms.

A preliminary study was conducted to identify serum samples with antibody to LAV II from populations in the U.S. at high risk for HIV infection. A total of 533 samples was tested using an EIA kit that included microwell strips prepared by Diagnostics Pasteur and components of the Genetic Systems LAV EIA. The samples included serum from 164 prostitutes in Miami, 181 Haitians in Belleglade, Florida, 164 gay men from San Francisco, and 24 seronegative people diagnosed as having AIDS.

Eighty-two of the 533 samples were positive for antibody to LAV I and LAV II. These samples were confirmed as LAV I positive by Western blot. The EIA results therefore represent cross-reactivity between the two viruses. One hundred and eighty-seven samples were positive for antibody to LAV I alone; and none of the samples was positive for LAV II alone.

The results of a research collaboration between the Food and Drug Administration, the Centers for Disease Control and Genetic Systems Corporation to study the epidemiology of LAV II in populations at high and low risk to develop HIV infection in the United States will also be presented.

THP.53 Rapid Progression of Infection of HIV Ab+ Transfusion Recipients from HIV-Infected Donors.

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We have followed 79 previous blood recipients of HIV-infected donors. Thirty-three were negative for anti-HIV and 46 were positive (Ab+). When first evaluated, 2 of the 46 Ab+ had ARC; none had AIDS. Six to eight months later, 10 had ARC (2 dead), 3 had AIDS (all dead). By the third visit, one more had ARC and two had died of AIDS. The total number of Ab+ recipients with disease was 14 (30%), 8 with ARC and 6 with AIDS. At the time of the initial visit, the frequency of abnormal laboratory results in recipients with (1) disease, (2) Ab+ but healthy, and (3) Ab- negative were as follows:
Absolute lymphocytes $< 1500/\mu l$: 57.1%, 34.4%, and 29%;
helper/suppressor ratio < 1.0: 85.7%, 78.1%, and 15.1%; and beta-2 microglobulin:78.6%, 56.3%, and 26.7%. Antibody to hepatitis B and CMV did not differ between HIV Ab+ and Ab- recipients. The results demonstrate rapid progression of infection in this group of high-risk recipients. On the initial visit the likelihood of infection and subsequent disease both correlated with the frequency of abnormal results in three tests, but the differences were of only moderate prognostic value for the individual case. All tests became more frequently abnormal when signs of disease appeared, but we do not have enough serial samples yet on healthy Ab+ patients to see whether trends in values will be more useful prognostically.

THP.54 AIDS in Women in the United States

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Women make up only 7% of all reported AIDS patients, but are an under-recognized source for heterosexual HIV transmission as well as the source for transmission to infants. As of January 23, 1987, 1,993 women had been reported with AIDS in the United States. Their mean age was 35.1 years; 52% were black, 27% white, and 20% Hispanic. Pneumocystis carinii pneumonia (PCP), the most commonly reported disease, occurred in 66% of women, while Kaposi's sarcoma (KS) was reported in only 3%. Fifty-one percent of female patients were intravenous drug abusers (IVDA); 27% were heterosexual contacts of persons with AIDS or at high risk for AIDS (21% were U.S.-born women, while 6% were born in countries where heterosexual transmission plays a major role); 10% had received transfusion with blood or blood products; for 11%, the means of transmission was undetermined. Compared with heterosexual male AIDS patients, women with AIDS were younger ($p < 0.01$), but were similar by race, residence, and disease. When female patients were analyzed by year of report, the following significant trends ($p<0.05$) were noted: an increase in U.S.-born heterosexual contact cases from 14% in 1982 to 26% in 1986; an increase in mean age from 30.0 years in 1981 to 35.6 years in 1986; a decrease in the proportion of females in the IVDA group between 1983 and 1986 from 59% to 48%; a decrease in foreign-born heterosexual patients from 18% to 5%. Increases in female AIDS patients in various risk groups were predictive of increases in pediatric patients whose mothers were in the same groups. The data indicate that heterosexual transmission of the AIDS virus to women is increasing. Continued monitoring of female AIDS cases will provide an indication of future trends in heterosexually-acquired and pediatric AIDS and information essential for prevention efforts.

THP.55 HIV Exposure in New York City Streetwalkers (Prostitutes)

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Eighty-one street walking prostitutes were studied in 1985, 1986, and 1987 to determine the prevalence of HIV infection. Two health care workers and a driver found the women as they worked. Age, number of years working, and history of drug abuse were determined. Consent was obtained and counselling was undertaken. Arms were examined for track marks while blood was drawn. Serum samples were screened for HIV antibodies by ELISA and confirmed by Western blot. The ages ranged from 19 to 37 (mean 25.) Time spent working as a prostitute on the streets ranged from two weeks to 20 years (mean 5.4 years.) Three of the subjects were men posing as women. One of them was also a drug user and was infected.

Of the 78 female subjects, twelve admitted to intravenous drug use and six (50%) were positive. Of the 65 female prostitutes who denied drug use five (7%) were positive. This could possibly represent heterosexual transmission. The overall seropositivity rate was 13 %. There was little difference between 1985, 1986, or 1987. These figures compare with 5% in Seattle, 25% in Miami, 6% in Athens and 88% in Rwanda. The incidence of this infection among New York City prostitutes does not seem to have increased greatly since 1982 when the principal investigator conducted a study of T cell subsets in 33 prostitutes.

funded by New York State Department of Health
HIV antibody tests performed by the New York City Department of Health

THP.56 Decreasing Survival in Recently Diagnosed AIDS-Related Kaposi's Sarcoma: PAUL VOLBERDING, D.W. FEIGAL, K. CUTLER, N. HEARST, San Francisco General Hospital, San Francisco, CA, USA

The survival of 162 consecutive AIDS/KS patients at San Francisco General Hospital was analyzed for variation related to the date of diagnosis. Patients were accrued between November 1980 and March 1984. 132 Patients are known to have died and 26 were surviving in January 1987. 47 patients with prior or concurrent opportunistic infections were excluded from analysis. Mean survival of quartiles of the cohort by diagnosis date were examined (Kaplan-Meier). Mean survival was longest in the early diagnosis group (1151 days) and prolonged in the subsequent quartiles (709,739,466 days respectively - $p<.01$). This worsening prognosis was even seen when patients with systemic signs (fevers, night sweats, weight loss) were excluded. Adjusting for other prognostic variables (helper/suppressor ratio, ESR and hematocrit) with Cox regressions also did not eliminate temporal trends in survival. KS treatment had no effect on these trends.

Decreasing survival in AIDS/KS could have resulted from changes in diagnostic practices (delayed diagnosis), increased viral virulence, changes in host resistance (eg. through changes in exposure to "cofactors" of immune deficiency) or in alterations in therapy. Adjustment of covariables suggests that the worsening prognosis of AIDS/KS is due to changes in HIV virulence or in host cofactors.

THP.57 Recreational Drug Use Does Not Cause AIDS Progression, the UCSF AIDS Registry Cohort:

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A clinical cohort of 1396 patients at the out-patient AIDS clinics of the teaching hospitals at the University of California, San Francisco, have been recruited to participate in a registry with periodic follow-up. At entry, 51% of study participants have AIDS, 36% have ARC, and the remainder are at high risk. At baseline 67% of the cohort reports smoking and 88% report alcohol use. Recreational drug use was classified into three categories:

	Less than once/year	once/month to once/year	More than once/month
Marijuana	60%	18%	22%
Cocaine	83%	13%	4%
IV Drug	95%	2%	3%
Nitrite	83%	11%	6%

Progression was defined as developing AIDS, CDC class IVC2 (ARC), lymphadenopathy syndrome or systemic symptoms characteristic of HIV infection. The relationship between recreational drug use and progression was examined with odds ratios comparing the lowest level of use to higher levels. 78 individuals were known to have progressed. No significant associations were found. Thus, although some types of substance use is associated with risk of seroconversion, once infected there is no evidence in this population that recreational drug use is a cofactor for progression.

THP.58 Severe HIV-Related Morbidity and Mortality in Cases not Meeting the CDC Surveillance Definition for AIDS.

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In 1981, the Centers for Disease Control (CDC) developed a surveillance case definition (SD) for AIDS, but it is now clear that the spectrum of disease associated with HIV infection is much broader than the original SD. In order to provide a better estimate of the true extent of severe morbidity and mortality (SMM) associated with HIV infection in Colorado, DCS investigated cases not meeting the SD but which seemed likely to result from HIV infection.

From May, 1982 to September, 1986, there were 239 cases of CDC-defined AIDS reported to DCS. During the same surveillance period, there were 33 cases of SMM reported and investigated. Five cases since have been diagnosed as CDC-defined AIDS. Nine of the remaining 28 are living and still may develop AIDS. The reasons for exclusion by the SD were: 17 cases (61%) the disease was not considered indicative of cellular immunodeficiency (CID); 7 (25%) a prior or concomitant immunosuppresive condition was present; and 4 (14%) the diagnosis was not reliably established. Diseases not considered indicative of CID included bacterial pneumonia, bacteremia, Candida endocarditis, Listeria meningitis, tuberculosis, disseminated sporotrichosis, Hodgkin's lymphoma, and AIDS-dementia complex. Therefore, there are at least 19 and as many as 28 cases of SMM outside the SD, representing 8% to 12% of reported AIDS cases. This estimate does not include cases of SMM possibly missed due to underreporting.

We conclude that the CDC SD for AIDS significantly underestimates SMM associated with HIV infection, that most cases of SMM are due to diseases not considered specifically indicative of CID, and that the CDC case definition should be expanded. In the meantime, inclusion of such cases and other manifestations of HIV infection in surveillance registries will provide a better estimate of the true spectrum of illness associated with HIV, as well as useful information about the natural history and prognosis of such patients.

THP.59 Analysing special features of a human lentivirus (HIV) infection and predicting the future development using computer based modeling (ASSP, AIDS Spread Simulation Program)

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The AIDS epidemic is a lentivirus infection, the unusually long and varying incubation period of which gives rise to several uncommon and insidious features in the epidemic's development, such as "transients" and delayed effects which may cause severe biases. These are described.

Indications are increasing for the possible role of macrophages as primary target cells for the HIV-infection, reason enough to consider the consequences of this hitherto underestimated virus survival in phagocytotic cells and what this would mean for the seroconversion latency. Many important conclusions follow from these assumptions.

Different ways of forecasting are compared to each other with regard to their efficacy for various purposes. The methods of curve fitting (extrapolation), analogous calculation (interpolation), mathematical modelling (formalising), and computer-based structural models (simulation) are applied to various countries and to short and long term predictions.

The development of a compartment-based computer program for simulating virus spread in large populations is described, the multinational modelling project ASSP (AIDS Spread Simulation Program).

THP.60 EVIDENCE FOR A CODETERMINANT OF AIDS ACQUIRED THROUGH RECEPTIVE ANAL INTERCOURSE

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A cohort of 537 homosexual HIV positive men in L.A. were followed for 18 months for changes in number of CD-4 cells. Seventy-one HIV antibody positive men developed AIDS. The mean slope in CD-4 cells was -.36/day (s.d.=.42) among men developing AIDS and -.01/day (s.d.=.01) among other seropositives. The mean slope by level of CD-4 cells at baseline was:

	Subsequent AIDS	Other Seropositives
< 200	-.25 (s.d. = .15)	.08 (s.d. = .20)
200-499	-.36 (s.d. = .38)	.04 (s.d. = .26)
> 500	-.46 (s.d. = .67)	-.05 (s.d. = .33)

The mean number of partners with whom cases practiced receptive anal intercourse the six months preceding baseline was 12.3 (s.d.=27.8) compared to 6.2 (s.d.=11.8) among other seropositives. The greater negative slope of CD-4 cells and the more frequent receptive anal intercourse among cases suggests that receptive anal intercourse is a route of entry for a factor(s) which increases the risk of developing AIDS among HIV seropositive men. This observation agrees with lab data that activation of CD-4 cells promotes lytic infection with HIV. It is also possible that men frequently practicing receptive anal intercourse were infected earlier and have progressed to AIDS by now. Follow-up of seroconverters to onset of AIDS should differentiate between these two alternate hypotheses. This observation provides a rationale for identifying agents acquired through receptive anal intercourse which stimulate a further decline in CD-4 cells and/or increase the risk of developing AIDS. By June data will be incorporated from an additional 1000 seropositive men in Baltimore, Chicago, and Pittsburgh.

THP.61 POSSIBLE CO-FACTORS OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION AMONG CENTRAL AFRICAN PATIENTS.

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Parasitic and viral serology were performed among 445 central African people (CAP) (sex ratio: 1:1). There were 4 groups matched for age and sex: 94 CAP seen in Brussels with a clinical HIV infection (P8r), 148 CAP living in a Central African city (K), 121 healthy CAP living in Brussels (H8r) and 82 CAP from a rural equatorial area (R). HIV antibodies were detected by ELISA and Western blot techniques. Antibodies for Trypanosomia brucei (T8), Plasmodium falciparum (PF) and Entamoeba histolytica (EH) were screened by immunofluorescence. Herpes type 1 (HSV1) and type II (HSV2) serology was performed by immunodot Enzyme Assay using monoclonal antibodies against HSV1 and HSV2 purified glycoprotein. HIV seroprevalence among the various groups was: 99% (P8r), 19% (K), 2% (H8r) and 0% (R). Previous parasitic infection was more frequently found among rural (R) than urban (K) people ($p < 0.001$ for all parasites) independly of their HIV serologic status. HSV1 was commonly found in all groups (83 to 93%). HSV2 antibodies were found in 82% of HIV positive CAP compared with 38% of the negative patients ($p < 0.001$). HIV and HSV2 prevalence was more marked among urban CAP (K) than rural people (respectively 19% vs 0% for HIV: $p < 0.001$; 50% vs 30% for HSV2: $p < 0.005$). Among CAP living in Brussels, HSV2 seropositivity was strongly correlated with HIV seropositivity ($p < 0.001$). HSV2 seropositivity was similar (41% vs 29%) among HIV negative urban or rural people.

This study shows that HSV2 seropositivity is strongly associated with HIV infection in Central Africa. Herpes type II could be a co-factor of HIV infection among promiscuous heterosexual Africans.

THP.62 *Epidemiologic observations and predictive factors for AIDS in a cohort of New York Homosexuals: 5 year follow-up.*

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104 Homosexual Volunteers (H/S) have been followed at 6 month intervals for 5 years. Of 56 volunteers seropositive for the human immunodeficiency virus (HIV-pos) at enlry into the study, 24 (42.8%) developed AIDS (1 in '82, 4 in '83, 8 in '84, 6 in '85, 5 in '86) and 8 developed ARC (14.3%). Of 48 HIV seronegative (HIV-neg) volunteers, 5 serconverted to an HIV-pos state but have remained asymptomatic. Cytomegalovirus (CMV), Enteroviruses (EV) were cultured with high but approximate equal frequency from both HIV-Pos and HIV-Neg volunteers from one or more of five sites (Blood, Semen, Urine, Throat, Rectum). Of multiple laboratory parameters performed prospectively at 6 month intervals, the combined appearance of acid-labile interferon Alpha (AL-IFN), disappearance of the Erythrocyte receptor for complement 3B (E-CR1) and appearance of a triple positive coombs test (positive for IgG, IgM, complement 3B) in an HIV-Pos individual invariably heralded progression towards overt AIDS within 6 to 27 months. This combination of parameters was not found in HIV-neg individuals including those with CMV-viremia.

Our observations suggest 1. Culture-positive CMV infection is frequent in N.Y.H.S. and is unrelated to the HIV infectious status. 2. The appearance of AL-IFN, triple positive direct Coombs'test and absence of E-CR1 in HIV-pos subjects reflects active pathogenic processes directly related to the progression towards AIDS that are not dependent on the reactivation of CMV.

THP.63 HIV Antibody Prevalence in Pregnant Haitian Women

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Pregnant women residing in an impoverished urban slum were screened for antibodies to HIV. Of 1240 women tested in 1986 by ELISA, 114 (9.2%) were positive and 104 (91%) were confirmed by Western blot with antibody to both env. and gag. proteins for an 8.4% confirmed antibody prevalence rate. Four additional ELISA positive specimens contained antibody to env. or gag. only and were considered indeterminant.

The prevalence rates of antibody in the 55% of married women was 11.5% versus 4.5% to 7.6% in women with less formal bonding to men. The prevalence rates by age groups were:

Age in Years		Age in Years		Age in Years	
15 - 19	7.5%	25 - 29	8.6%	35 - 39	8.9%.
20 - 24	11.2%	30 - 34	6.5%		

The 8.4% prevalence rate of WB confirmed antibody to HIV in 1986 was only slightly higher than the 7.6% rate observed in a sample of 533 mothers of young infants bled in 1982. Aliquots of sera tested in 1982 were retested with second generation ELISA and WB assays and found to give virtually identical results. Thus, the rate of increase in HIV antibody prevalence in this population does not appear to be as rapid as reported in other high risk populations in Africa or in the U.S.

THP.64 Incidence of AIDS Related Clinical Manifestations in a Large Cohort of Gay/Bisexual Men

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Few studies have documented the incidence of new AIDS related clinical manifestations. We analyzed these clinical features in a prospective study of gay/bisexual men examined semiannually. Combinations of symptoms, physical signs, and lab abnormalities that correlated best with a low CD4 count or eventual AIDS were used as an index of clinical involvement. Within 18 months of follow up, at least 231 HIV+ men newly developed substantial clinical involvement (a high clinical index score). Life table probabilities of reaching this threshold score are shown for men who were HIV+ (Initial N=1809) and men who were HIV- (Initial N=2864) throughout the interval.

% with substantial AIDS related clinical involvement

	At entry	Newly reached in: 1st 6 mo	2nd 6 mo	3rd 6 mo	Cumulative (%)
HIV(-)	1.3	0.7	0.9	1.1	2.7
HIV(+)	5.3	4.1	6.0	8.1	17.2
(+), Entry CD4=700+	3.2	2.4	1.9	6.7	10.8
(+), 400-699	3.7	2.7	6.5	7.4	16.1
(+), 0-399	11.9	7.8	14.1	14.4	32.3

The 18 month cumulative incidence of substantial clinical involvement in seropositives was 17.2% and varied with initial CD4 count from 10.8% to 32.3%. The data also suggest that the probability of reaching a high clinical index score in a 6 month period was not constant but rose with time regardless of initial CD4 count. It is not yet clear whether this steadily increasing incidence of AIDS related manifestations correlates with the likelihood and rate of progression to AIDS.

THP.65 Reactivity of Ghanaian Sera to Human Immunodeficiency Virus (HIV) and Simian T-Lymphotropic Virus III (STLV-III).

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Acquired immunodeficiency syndrome (AIDS) in Africa which was previously confined to the East and Central African countries is now in West Africa. The disease in Africa may take an epidemic character if measures are not taken to check its spread. Prevalence rates and the risk groups therefore need to be assessed and identified. Detection of antibodies (Abs.) to HIV and STLV-III antigens (Ags.) was carried out in human sera from blood donors, prostitutes, sickle cell disease patients and others. The ELISA and Immunofluorescence (IF) techniques were used for HIV Ags. and IF for STLV-III.

Out of a total of 997 samples (226 from prostitutes) examined for HIV and 737 for STLV-III. Abs. 93 including 57 prostitutes were positive for HIV and 18 for STLV-III. Abs. Some of the sera reacted better to STLV-III Ags. Western blotting test also confirmed these differences.

Reports on Senegalese showed that some reacted to STLV-III Ags.without any disease. The Ghanaians reacting to STLV-III showed disease. The Western blotting reaction suggests that some of the Ghanaians have been exposed to a virus which may be closely related to STLV-III.

A new virus HTLV-IV has been reported from Senegal. Retrovirus infection in Africa may therefore be more varied than in the Western Hemisphere. Isolation and characterization of local strains of HIV and their inclusion in tests as Ags. may be necessary to determine the incidence rates in some of these African countries. Work is currently going on in this direction.

THP.66 Epidemiologic Characteristics of Women with AIDS in New York City

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The annual death rate due to AIDS per 100,000 women 25-44 years of age in New York City (NYC) has increased from 0.4 in 1981 to 15 in 1986 (based on the AIDS case registry). In order to identify women most at risk for infection, the characteristics of women with AIDS in NYC were determined through an analysis of surveillance data. The 867 female cases in NYC represent 10% of all NYC cases and 45% of all female cases reported nationally. In 1986 the incidence of AIDS per 100,000 women 25-44 years of age in NYC was 48 for blacks, 8.5 for whites, and 36 for Hispanics. The major risk behavior reported was IV drug use (IVDU) by the women (61%) or their sex partners (18%). In addition, 3% were sex partners of other at risk individuals, 4.5% were from countries where risks are unclear, 3.5% were recipients of blood or blood products, 2.5% had no identified risk factor(NIR), 2.5% were lost to follow-up, and 5% were under investigation. The average age of the IVDUs, the sex partners of at risk individuals, and women from countries where risks are unclear was 33, while that of transfusion recipients was 50, and that of the NIRs was 38. In NYC, 51% of the female IVDUs with AIDS are black, 15% are white, and 34% are Hispanic. Among the female sex partners of at risk individuals, 41% are black, 16% are white, and 43% are Hispanic. Of the female transfusion cases, 25% are black, 68% are white, and 7% are Hispanic. In 1985 AIDS was the leading cause of death among women 25 to 29 years of age in NYC. These data show that in NYC AIDS is a leading cause of morbidity and mortality among women 25-44 years of age and that women who are IVDUs or sex partners of IVDUs are at greatest risk of infection with HIV.

THP.67 Evidence for a Causal Association Between HIV Infection and Increasing Tuberculosis Incidence in New York City.

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Concurrent with the AIDS epidemic, New York City tuberculosis (TB) incidence rates have increased 60%, from 20/100,000 in 1980 to 32/100,000 in 1986. The groups with the largest increase in incidence have been males aged 25-44 who are black (from 96 to 231 cases per 100,000) and Hispanic (from 35 to 103 cases per 100,000). These groups also account for 52% of all NYC AIDS cases aged 25-44. In order to investigate the association between HIV infection and TB, two studies were undertaken: we matched the NYC TB and AIDS surveillance registries to determine TB incidence among AIDS cases; and we used the TB registry to determine TB incidence in 519 intravenous drug users (IVDU) enrolled in a study of risk factors for HIV infection and AIDS. Of 6,365 AIDS cases diagnosed from 1982 through April, 1986, 266 (4.2%) also matched with the TB registry. Compared to AIDS cases with the lowest risk for TB (whites and gay men), groups at high risk for TB were blacks (OR 4.5,95% CI=3.2-6.2), Hispanics (OR 2.9 95% CI=2.0-4.3), and IVDU (OR 3.6 95% CI=2.7-4.8). Among the 519 IVDU, 12 cases of TB were identified and all occured among 279 persons with serological evidence of HIV infection or clinical AIDS (p<.001). These data support the hypotheses that persons co-infected with TB and HIV are at a higher risk of TB disease than similar persons without HIV infection, and that AIDS and HIV infection are causally related to increasing TB incidence in NYC. Areas with populations that have a high prevalence of TB and HIV infection should anticipate similar increasing TB trends and plan prevention and control strategies accordingly.

THP.68 Genital Ulceration As a Risk Factor For Human Immunodeficiency Virus Infection In Kenya

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We studied 115 heterosexual men with genital ulcers in a sexually transmitted diseases clinic in Nairobi, Kenya and found the prevalence of serum antibody to human immunodeficiency virus (HIV) in this population was 16.5% which is higher than the prevalence reported in other groups of men in Kenya. Our results also indicate that genital ulcer disease may increase risk of infection with HIV. Of 19 men with antibody to HIV, 12 (63.2%) reported previous genital ulcers, versus 30 (31.3%) of the 96 men without antibody to HIV (p=.008). Logistic regression analysis showed that antibody was significantly associated with a past history of genital ulcers (p=.03, odds ratio 3.71, 95% confidence limits =1.14-11.42) but not current or previous episodes of other sexually transmitted diseases, or the etiology of current genital ulcers. Genital ulcers are a common sexually transmitted disease in Africa and may contribute to the increased risk for HIV apparent among heterosexuals in this region.

THP.69 Cohort study of New York City male homosexuals, 1981-86.
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Eighty-six male homosexuals who participated as controls in case-control studies of AIDS have been followed prospectively. Minimum cumulative HIV infection was 30% (21/69) in 1981-2, 39% in 1982-3 (31/79), 48% (41/85) in 1984, 48% (41/86)in 1985, and 51% (44/86) in 1986. Seven cases of AIDS have occurred. The longest follow-up of AIDS-free, HIV-infected subjects was for 8 persons who were seropositive in 1981-2. The median OKT4/OKT8 ratio of these 8 in 1986 was 0.36 (mean OKT4 cells=421, SD=178 cells/mm^3); 7 of the 8 have shown continual declines in OKT4/OKT8 ratios. Another 8 AIDS-free subjects have seroconverted. In the combined group of 8 subjects who were seropositive on enlistment and 8 seroconverters mean OKT4 cell counts declined with duration of follow-up. Interviews revealed that 12/65 (18%) subjects had been celibate in the 6 months prior to interview in 1986 and an additional 3 (5%) had adopted strict "safe sex" guidelines including 100% use of condoms during anal intercourse. Although the cohort as a whole showed a decline in the number of sexual partners between 1985 and 1986, subjects who eliminated all risk of sexually-transmitted AIDS were significantly more likely to be seronegative than those who continued to place themselves or others at risk. These data suggest (a) that duration of infection is associated with severity of AIDS-related immunologic abnormalities, and (b) that educational efforts to reduce HIV transmission among homosexual men have not strongly affected those who have been so active sexually as to have become HIV infected.

THP.70 AIDS in New York State Prison Inmates
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Through January 15, 1987, 347 cases of AIDS had been reported among prison inmates in New York State correctional facilities. This represents approximately half of the inmate AIDS cases in U.S. state and federal systems. An analysis of epidemiologic data on these cases has shown an increase in cases yearly from 2 in 1981 to 107 in 1986, with an incidence of 302 cases per 100,000 inmates per year over the past 2 years. Case ages ranged from 18 to 59 years: 335 (97%) were male, 12 (3%) were female. Forty-six percent were hispanic, 39% black and 14% white. Pneumocystis carinii pneumonia (76%) and other opportunistic infections (17%) were the most common diagnoses, while Kaposi's sarcoma was rare (3%). To date, 228 have died and AIDS has become the leading cause of death among inmates causing > 50% of deaths.

IV drug use (97%) was the major risk factor and most inmates had lived in the NYC area prior to incarceration. Only 12% gave a history of homo-/bisexuality and 80% of these used IV drugs. A comparison of 52 cases with 101 matched controls, showed that inmates who developed AIDS had significantly ($p > .01$) lower entrance WBC counts, hematocrit, and albumin, and higher globulin and SGOT values. Logistic regression analysis of the 52 cases and 196 random controls showed previous IV drug use, low WBC count, elevated serum SGOT and globulin, and race to be risk factors for development of AIDS. No long term inmates (≥7 years of continuous state incarceration or admission prior to, 1978) have developed AIDS, but a more definitive study on risk of transmission during incarceration is needed.

THP.71 Evaluation of HIV IgM and Antigen Assays for Determination of Perinatal Infection with HIV.
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No serologic assays are available to distinguish HIV infection during infancy from passive maternal antibodies against HIV. Coded sera from 14 third-trimester pregnant women and serial specimens from their offspring (up to 3-9 mo. of age) were tested blindly for HIV-p24 antigen (HIV-Ag), for anti-HIV IgG and IgM by whole virus Western Blot (WB) and by ELISA using recombinant env and gag proteins. By conventional whole virus ELISA and WB, 8 mother-infant sets were positive and 6 sets negative. There was serologic evidence of infection in two sick babies; one with HIV-Ag env-IgM(6 months), env-IgG and gag-IgG; the other had no HIV-Ag but transient gag-IgM (age 1 mo) and env-IgM (ages 1-2 mo) with a subsequent increase in gag-IgG and env-IgG (ages 2-6 mo). A third baby had no HIV-Ag or IgM by ELISA, but at ages 2-6 mo did have a modest increase in gag-IgG, env-IgG, WB-IgG (p17 p24 p55). The remaining 5 infants of seropositive mothers had no HIV-Ag, no IgM by ELISA, and declining IgG by ELISA and WB: one of them is symptomatic. All 14 babies had faint WB-IgM bands especially at p24. Two seronegative mothers had env-IgM and gag-IgM without HIV-Ag, IgG, subsequent seroconverison (after 3-6 mo) or evidence of HIV in their babies. These data suggest either that relatively few (perhaps 2/8) babies of HIV-seropositive mothers are infected or that HIV assays for IgM and Ag require improved sensitivity and specificity to distinguish HIV infected babies during the first 6 months of life.

THP.72 Heterosexual Transmission of AIDS in Canada - National Surveillance
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Between February 1982 and January 1987, 843 adult AIDS cases were reported to the national surveillance program in Canada. Risk factor data indicate that although homosexual men have accounted for an increasing proportion of the total reported cases, heterosexual AIDS cases were observed very early in the course of the epidemic, and have been reported consistently over time. In 3.6 percent of all AIDS cases reported, heterosexual activity was considered the probable risk factor for HIV infection. Nine cases were white males aged 35-57 years (median 45 years); 11 were white females aged 24-58 years (median 40 years);and 10 were Haitian females aged 25-32 years (median 29 years), who had emigrated to Canada prior to 1980. Six of the males reported sexual activity with female prostitutes, two had multiple female sex partners, and one had a sex partner who developed AIDS. The female cases were attributed to sexual activity with individuals who later developed AIDS or whose lifestyle included activities known to increase the risk of exposure to HIV.

The first AIDS case in Canada attributed to heterosexual activity was diagnosed in 1981. In each of the five subsequent years to the end of 1986, 2 percent to 4 percent of AIDS cases reported this risk factor. These surveillance data indicate that heterosexual transmission is not a new phenomenon in this country and this mode of transmission has accounted for a small but consistent proportion of AIDS cases diagnosed each year. Bidirectional sexual transmission of the infection is supported by the sex distribution observed among these cases. The cases were reported from the large urban centres where HIV infection is most prevalent.

THP.73 Cohort Study of HIV-seronegative Homosexual Men: Predictors of Seroconversion and Clinical Course of Early HIV Infection
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Most data on factors associated with HIV infection in homosexual men(HM) are based on case control studies comparing HIV-seropositive(HIV+) with HIV-seronegative(HIV-) men. We have followed a cohort of HIV-HM and prospectively examined factors associated with HIV seroconversion. Among 92 HM without clinical problems suggestive of HIV infection examined in 1982-85, 25(27%) were HIV+. Of 67 HIV-HM, 45(67%) were followed for 18-47 mo(med-ian 39 mo). Among these, 14(33%) became HIV+ after 2-44 mo(median 21 mo). Compared with the 29 persistently HIV-HM, the 14 ser-oconverters had more sex partners in the interim before serocon-version(median 6 vs 2 partners,P=0.017); more commonly had a new partner in the preceding 1 mo(11/13 vs 11/28,P=0.009); and more commonly participated in receptive anal intercourse with rectal ejaculation(10/11 vs 13/28,P=0.012). There was no difference in overall secretion exchange during sex(11/12 vs 23/29, P=NS). Nine seroconverters developed generalized lymphadenopathy(GL)(detected when first HIV+ in 6, and 3-24 mo later in 3). GL persisted >3 mo in 8. These results support the hypothesis that receptive anal intercourse and increased numbers of sexual partners are specific risk factors for acquisition of HIV in HM, and suggest that most recent HIV infections are associated with clinical findings.

THP.74 Statistical analysis of European AIDS surveillance data: trends and predictions.
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European AIDS surveillance data have been analysed statistically to assess incidence trends and to provide short-term predictions. After adjustment for estimated reporting delays, the data (cases per half-year of diagnosis) were fitted to an exponential model. For the European Community (E.C.) as a whole (90% of European cases reported) and for 10 individual countries (those with at least 50 reported cases by 30 June 1986), the temporal evolution of the epidemic was assessed by performing regression analysis over a succession of time intervals (windows). For 3 countries, separate analyses have also been carried out for the two main risk groups (homo/bi-sexual men; IV drug abusers). Predictions to mid-1988 have been made by extrapolation based on estimated current doubling times. Available results are based on data reported as of 30 June 1986. Reporting delays were found to show considerable between-country variation. For the E.C. overall and for most individual countries (with the exception of Italy, Spain and Switzerland), doubling times were found to be increasing with time (for the E.C., from 6.5 months to 9.4 months over 2.5 years), as observed in the U.S.A. Preliminary analyses by risk group strongly suggest that the different evolutions in Italy and Spain may be related to the much larger proportion of cases among IV drug abusers in these countries, but this result is not yet statistically significant. Estimates of current doubling times range from 4.3 months (Italy) to 17.7 months (Denmark). If the doubling time for the E.C. as a whole were to remain at its currently estimated value of 9.4 over the next two years, the cumulated total of cases diagnosed in the E.C. could reach around 19,000 by mid-1988. Hopefully, this should represent an overestimate as doubling times are likely to continue to increase. Results will be up-dated to include all cases reported as of 31 December 1986.

THP.75 Seroepidemiological Study of HIV1 and HIV2 Infection in Guinea-Conakry

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LAV2/HIV2 is a human retrovirus recently described in patients from Western Africa. To evaluate the presence of HIV infection in Guinea-Conakry, sera were collected, in october 1986, from 914 subjects (518 males, 396 females) in two areas - Conakry, the capital (756 subjects) and Labbe, a city of the north-east country (158 subjects). Sera were tested for antibodies to HIV1 (HIV1-Ab) and HIV2 (HIV2-Ab) by Elisa (Diagnostics Pasteur) and confirmed by Western blot(WB)

In Conakry, HIV seropositivity was found in 8/756 subjects : 2/81 were patients hospitalized in medicine ward, 5/121 patients with tuberculosis and 1/277 was hospital health-care worker; 6 were HIV1-Ab @ and 2 HIV2-Ab @. No HIV-Ab were found neither in 167 females attending gynecology/obstetrical clinics nor in 110 military recruits. In Labbe, 1 hospitalized patient had HIV1-Ab @ while 127 subjects from general population were HIV seronegative.

This study shows a prevalence of HIV infection of - 1% (9/914) in this tested population; the highest rate was found in tuberculosis patients (4/121). Besides, 4 sera were repeatedely HIV1-Ab @ by Elisa; when analysed by WB, they exhibited only antibodies to gag (p18-p25-p40-p56) and pol (p34-p38) gene products with no Ab to the envelope glycoproteins of HIV1 (gp160.110.41) or HIV2 (gp130.105). Presence in Guinea of both HIV1 and HIV2 is evidenced by this study; a low prevalence of HIV infection in countries as Guinea is an argument to undertake rapidly management for prevention of transmission, such as blood-bank screening, before the extent of retroviral infection.

We thank C.E. DE TSERCLAES for assistance.

THP.76 Predictives of AIDS in a clinical cohort of HIV infected patients.

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Since 1983, over 500 patients with confirmed HIV infection, but initially without AIDS, have been followed. Of these patients, 22 developed clinical AIDS in follow-up of 1 to 3 years. Of these, 14 had ARC at their examination 6 had lymphadenopathy, and 2 were asymptomatic. To determine the power of a variety of laboratory tests to predict the development of AIDS, a matched case-control study was performed. Each patient who developed AIDS in the course of follow-up was matched with a control who had the same initial clinical findings at that time. These data were analyzed using matched logistic regression analysis. The variables analysed were the numbers of white blood cells, lymphocytes, T4 and T8 cells, the levels of serum B2 microglobuline IgG and IgA level. The most important predictor for the development of AIDS was the absolute number of T-helper cells(T4) followed by the level of beta2-microglobuline(B2). From univariate analysis, the crude odds ratios for the development of AIDS were .08 for T4 > 400 vs. T4 < 400(p=.02) and .18 for B2 < 350 vs B2 > 350 (p=.09). When both variables were entered simultaneously in the logistic model, the regression coefficients were not much changed although the significance levels associated with them were higher. Thus, level of beta2-microglobuline appears to provide more information than does T-helper count alone concerning the risk of developing AIDS, but larger sample sizes will be needed to confirm this hypothesis. Linear regression analysis demonstrated that the most important predictor of the level of T4 cells 6 months after the initial clinical visit was the level of T4 at the initial visit but the level of B2 microglobuline also had a predictive value.

THP.77 Is HIV Infection Increasing in the United States? A Review of Evidence from Sentinel Populations

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It is widely assumed, though without evidence, that human immunodeficiency virus (HIV) infection is increasing in the United States, since reported AIDS cases continue to increase. We reviewed divergent infection trend information from two large volunteer groups: military recruit applicants and American Red Cross blood donors. To date, approximately 900,000 recruits and 7,000,000 donors have been tested for HIV antibody by ELISA and, when reactive, confirmed by Western blot. Overall, 1.5 of every 1,000 recruits tested were positive (1.2/1,000 when sex adjusted). Infection rates vary by age (17-20 yrs., 0.6/1,000; 21-25 yrs., 2.5/1000; ≥ 26 yrs., 4.1/1,000), sex (males, 1.7/1,000; females, 0.7/1,000), race/ethnicity (whites, 0.8/1,000; blacks, 4.1/1,000; Hispanics, 2.1/1,000), and geographic area. However, during the observation period, the level of infection did not significantly change either in the aggregate or by demographic or geographic subgroup. Blood donors averaged 0.23 per 1,000 tested, varying by sex (males, 0.29/1,000; females, 0.07/1,000) and geographic area. Detection rates decreased from the initial 0.38/1,000 level, due to the elimination of previous positives among repeat donors. However, preliminary analyses of first-time donors suggest that rates in that group doubled over a 1-year period. Reasons for the apparent divergence between recruit and new donor trends are unclear. The groups differ in socioeconomic, geographic, and age composition; degree of exclusion of persons with exposure risks; and likelihood that some participated specifically to determine their HIV-antibody status. Evaluation of these trends by a monitoring system independent of self-selection bias, such as the sentinel hospital based surveillance, is essential.

THP.78 Prevalence of HIV- and HTLV IV-infections in Angola.

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A seroepidemiological study of HIV and HTLV-IV infection was performed in the capital Luanda and in the Cabinda district, which is situated as an enclave between Kongo and Zaire, in Angola in October 1986. Until October 1986 five cases of AIDS had been registered in Angola. During this study another three cases with clinical AIDS, as defined by the Bangui criteria, were found and confirmed by HIV-serology. Sera from groups of healthy persons and groups of patients were screened for HIV-antibodies by ELISA(Organon-Teknika) and for HTLV IV-antibodies by immunofluorescence on HTLV IV-infected HUT-78 cells or by dot immunobinding. All screening positive sera were tested by Western blotting with HIV- and/or HTLV IV-antigens. In Luanda HIV-antibodies were demonstrated in 2/452 (0.4%) male blood donors, in 1/357 (0.3%) pregnant women, in 1/100 (1%) patients hospitalized with tuberculosis, in 4/94 (4%) patients at medicine wards and in 0/22 women hospitalized with pelvic infections. Two known male AIDS-patients and two of their three wifes were also HIV-seropositive. In Cabinda 4/38 (11%) women at a maternity ward were found HIV-seropositive, but only 1/52 (2%) of other hospitalized patients and none of 31 male blood donors or 59 healthy persons in a village on the border of Zaire. Specific antibodies to HTLV IV were not found in any of 177 blood donors or 100 patients from Luanda. However, eight out of nine HIV positive sera crossreacted with HTLV IV by immunofluorescence and with HTLV IV gag proteins by Western blotting. HIV infection exists in Angola, but not to the same high extent as in some neighbouring countries in Central Africa.

THP.79 Differential Participation Rates and Epidemiologic Estimates of AIDS.

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Studies on AIDS among gay men and IV drug users show a high degree of variability in prevalence rates of HIV infection, ARC and AIDS, and it is clear that a significant amount of this variation is due to methodological biases, including recruitment procedures and attrition rates. This presentation begins to address this problem by describing the relationship between differential rates of participation and attrition and ethnic and sexual behavior factors in a gay male NYC cohort of 745 men recruited for a longitudinal AIDS study in 1985. This group was selected from diverse community channels with special efforts made to recruit black and Hispanic men. Even with these efforts black and Hispanics made up only 13% of the sample. Surveillance data at that time indicated that 33% of gay/bisexual AIDS cases in NYC were minority group members. This initial bias was compounded by differential attrition rates of whites and non-whites at one year follow-up. The overall attrition rate was 11%. However, black and Hispanic men were more than three times as likely to be lost to follow-up (25%) as were white men (8%) due to more often refusing to be reinterviewed, posing insolvable logistics problems and being ill or dead due to AIDS. This difference is problematic because men who declined to be reinterviewed reported having more than twice as many sex partners in the year before they learned about AIDS (mean=241) than did men who were interviewed at both times (mean=108). These men were also more than five times less likely to have enrolled in the HIV antibody evaluation component of the study compared to those who were reinterviewed (9% vs 50% respectively). These results suggest that the highest risk individuals, the highest rates of HIV infection, and the highest rates of AIDS are to be found in the subset of individuals who never enroll or are unwilling to continue participation in behavioral and serologic AIDS studies.

THP.80 IV Drug Abusers with Homosexual Activity: An Ethnographic Study of Subtypes of Men with Two Risk Factors

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Men who are IV drug abusers (IVDA) and have male sexual partners are of special interest in terms of the epidemiology and prevention of HIV transmission since they are at high risk of exposure through two independent mechanisms and may serve as a link to heterosexual transmission. A methodologically rigorous estimation of the absolute numbers, social characteristics, and behaviors of such men is difficult to obtain. We will present information obtained from several ethnographic studies which support the existence of at least 2 subgroups of such men:

1. Men with primary identification with the IVDA subculture: Such men share the general characteristics of inner city IVDAs, including lower SES, chronic use of drugs such as heroin, regular sexual contact but a low level of social identity with the gay subculture, homosexual contacts are highly stigmatized and often are furtive and include the exchange of money, poorly informed about the sexual transmission of HIV and are unlikely to be reached through research and educational outreach to the gay community.

2. Men with primary identification with the gay subculture: Such men are relatively rare and tend to be older and of higher SES than the first group of men. They are relatively well informed about the sexual transmission of HIV but may be uninformed about the risks of needle sharing. Their IVDA tends to be of an episodic and recreational nature, often associated with sexual activities or gay social settings. Drugs used IV tend to be cocaine, amphetamines and MDA rather than heroin and they tend to view messages aimed at IVDAs as irrelevant.

Designing interventions aimed at these two subgroups appears warranted.

THP.81 AIDS Surveillance in Europe

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A WHO Collaborating Centre on AIDS was set up in April 1984 at Claude Bernard Hospital in Paris (France) in order to collect epidemiological information from the AIDS surveillance systems in European countries. The Centre uses the CDC case definition; the data are provided by one source per country which is recognized by the respective national health authorities, and quarterly reports of the situation are published. By December 1986, 27 countries were reporting to the Centre. Although France reports the greatest number of cases (1350), the rates per million population are higher in Switzerland and Denmark (29.5 and 25.7). The trends of these rates show that most countries are now facing an epidemic. Overall, the majority of cases have been diagnosed among homosexuals (69%) but a steady increase is noted in the IVDA group (14%). There are geographic variations between the northern countries (predominance of homosexuals) and southern countries (predominance of IVDA). The majority of the paediatric cases are children whose mothers belong to one of the groups highly represented in the country of diagnosis. This network enables comparative views on specific problems (e.g. public health), initiation of collaborative studies, and information exchange for ongoing studies in the European region. An update of the situation by March 1987 will be presented.

THP.82 Risk of Heterosexual and perinatal transmission of Human Immunodeficiency Virus Infection (HIV) Among Spouses and Children of Hemophilic Patients with AIDS

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The risk of heterosexual and perinatal transmission of HIV infection is a major public health concern and still not fully understood. From 1981 to 1986 ten hemophiliacs were diagnosed to have AIDS with a latency period of ranging from 27 to 60 months (median of 36 months) as determined by the time from the seroconversion to HIV to the onset of AIDS. Their spouses and children who were conceived and born during the latency period of AIDS are at risk for HIV infection. Five wives and 4 children conceived during the time of their fathers' seroconversion to HIV were identified and tested for HIV antibody and immune status following the diagnosis of AIDS were established. Four of 5 wives were negative for HIV antibody with normal ranges of T4 (729±133/cmm mean±s.d.), T8 (430±152),and T4/T8 ratio(2.0±0.6). One spouse with a history of multiple sclerosis and immunosuppressive therapy, but no other risk factors for HIV infection, was tested positve for HIV antibody by ELISA and Western blot technic, and reduced T4 (82/cmm) count while remaining asymptomatic. Four children from 2 families conceived while their fathers were positive for HIV antibody were also seronegative for HIV while maintaining normal T4 and T8 counts. This finding suggests that a large number of hemophiliacs through their exposure to contaminated clotting factors are at risk for HIV infection, but the risk of transmission to their spouses and children conceived during the the period of seroconversion to HIV may be small. Nevertheless, until the real magnitude of this risk is defined, a judicious measure to prevent the risk of transmission is warranted.

THP.83 Opportunistic Diseases in Florida AIDS Cases: Risk Groups and Time Trends

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As of January 23, 1987, 2,050 cases of AIDS meeting the Centers for Disease Control definition were reported from Florida, of which 1,213 were homosexual/bisexual (HO/BI), 286 IV drug users, 251 persons born in "No Identified Risk" (NIR) countries, and 300 in other risk groups. For the total cases, 2,569 opportunistic diseases were reliably diagnosed. An analysis of surveillance data was conducted to describe changes in the occurrence of selected opportunistic diseases by risk group. Five diseases accounted for 86% of the total: Pneumocystis carinii pneumonia (PCP) 46%, Kaposi's sarcoma (KS) 16%, candida esophagitis (GC) 14%, toxoplasmoais (TP) 5%, and cytomegalovirus (CMV) 5%. The distribution of each disease within the three largest risk groups was as follows:

	Disease				
Risk Group	PCP (N=1201)	KS (N=406)	GC (N=405)	TP (N=162)	CMV (N=161)
Homosexual/Bisexual Male	56%	76%	42%	41%	50%
IV Drug User	13%	3%	19%	14%	8%
Persons Born NIR Countries	9%	6%	14%	25%	10%

From 1981-1986, the cumulative incidence of KS showed a slight decrease relative to the other opportunistic diseases (17 to 14%), a decline which was most pronounced among persons born in NIR countries. PCP increased over this time period (32 to 48%), mostly due to an increase of PCP in HO/BI males. GC showed a decrease after 1983, primarily as a result of a decline among persons born in NIR countries. Persons born in NIR countries also showed a decrease in TP and CMV. The clinical diagnosis and treatment of AIDS will benefit from maintaining a high index of suspicion for risk group-specific opportunistic diseases.

THP.84 Rapid spread of HIV infection in a rural district in North Uganda.

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Spread of HIV infection in Central Africa is rapidly increasing: a rising number of AIDS cases and a high prevalence of anti-HIV antibodies have been recently demonstrated both in urban and rural areas. Results of a sero-epidemiological survey in a rural district in North Uganda (East Alcholi) are reported. During 1984 sera were collected from 111 subjects living in a rural area of the disctrict and mainly affected with malaria or dracunculiasis. In 1986 another group of sera was obtained from 491 subjects including 50 inpatients affected with TB, 246 inhabitants of 2 small villages, 37 soldiers from an army settlement, 158 members of 3 hospitals staffs of the district (Kitgum, St. Joseph and Kalongo hospitals). Sera were tested by 2 commercially available ELISA methods and by IFA. In the ones resulting positive by at least one method, W.B. confirmation was sought for. In the first group (1983-84), only 1 out of 4 ELISA positive samples was WB confirmed (0.9%). In the second group (1986), overall positivity rate was 13.2%. No significant differences were observed between the different groups: soldiers 17%, pregnant women 12%, TB patients 10%, Hospital staff 13.2%, rural population 13.8%. The great increase of anti-HIV seropositivity in such a short time indicate the dramatic spread of the epidemic even in remote rural areas of Central Africa.

THP.85 HIV antibodies in blood bank donors, hemophiliacs, homosexual men, prostitutes and hemodialysis patients, in Brasil

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In 22,245 serum samples from São Paulo City blood bank donors obtained from June 1985 to November 1986, studied by HIV ELISA test and H9 control plates (Electro-Nucleonics) and Abbott HIV Confirmatory EIA, 40 (0.18%) were positive. In 1986, 73.21% (41/56) of patients with hemophilia A (treated with local and/or imported factor VIII concentrate) and 30.9% (17/55) of homosexual men from São Paulo were positive. No antibodies to HIV were found in 176 prostitutes from São Paulo. The study of 938 serum samples from polytransfused hemodialysis patients from São Paulo, tested retrospectively from 1986 to 1976,revealed that 1.61% (2/124) of the samples obtained in 1986 and 4.80% (5/104) in 1985 were positive; no positiveness was observed in sera from 1984 or prior to it. There were 6.18% (58/938) of false positive reactions due to antibodies against H9 antigens.Serum samples obtained from patients with hemophilia A in Rio de Janeiro City during 1983-1984 revealed 98.24% (56/57) of positiveness to HIV antibodies (treated mainly with factor VIII concentrate prepared from locally collected plasma).

THP.86 Tuberculosis and the Acquired Immunodeficiency Syndrome - Florida

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To determine the impact of AIDS on tuberculosis morbidity in Florida, the State AIDS and tuberculosis registries were matched. Of the first 1,094 AIDS cases reported from Florida through December 1985, 109 (10%) were determined to also have had tuberculosis. Tuberculosis preceded the diagnosis of AIDS in 57%, was concurrent with in 28% and followed the diagnosis of AIDS in 16%. Patients with AIDS and tuberculosis (AIDS/TB) were younger than AIDS patients without tuberculosis (AIDS/non-TB) (median age 34 years vs. 35 years); were more likely to be black (81% vs. 21%) and less likely to be white (11% vs. 50%); were less likely to be homosexual/bisexual men (21% vs. 62%); and were more likely to be foreign-born (60%) than AIDS/non-TB patients (25%). The 105 tuberculosis patients with AIDS (TB/AIDS) who were reported to have tuberculosis from 1981 to 1985 were compared to the 7,136 tuberculosis patients without AIDS (TB/non-AIDS) reported during the same period. TB/AIDS patients were found to be younger (median 33 years vs. 49 years) and were more likely to be black (79% vs. 51%) than TB/non-AIDS patients. They were less likely to have pulmonary tuberculosis (62% vs. 89%); were less likely to have pleural tuberculosis (0.1% vs. 3.0%); and were more likely to have lymphatic (19% vs. 2.3%) and miliary tuberculosis (9.5% vs. 1.3%) than TB/non-AIDS patients. These data suggest that tuberculosis is common in AIDS patients in Florida and that AIDS/TB patients differ in many demographic and clinical aspects from AIDS/non-TB patients and TB/non-AIDS patients.

THP.87 Descriptive Epidemiology of Acquired Immune Deficiency Syndrome Cases Among Native Born Black Persons in the United States Reported June 5, 1981- April 14, 1986

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Research was undertaken to determine the descriptive epidemiology of AIDS cases among native Black Americans. From June 5, 1981 - April 14, 1986, 4,362 cases of AIDS were reported among Black persons born in the U.S. 4,195 were adults/adolescents, and 167 children. 2,510 of these are known to have died, a case fatality rate of 57.5%. Among adult patients, 41% were gay/bisexual males, and 39.31% intravenous drug abusers. Patients with Pneumocystis carinii Pneumonia only accounted for 65% of all cases Over 40% resided inthe North-East SMSA. The annual incidence rate in this selected sub-population of Black cases was 0.85 cases per 100,000. Comparison with a control group consisting of the remaining 15,198 cases as of April 14, 1986 yielded statistically significant differences: the study group included 9.1% more females; 2.4% fewer cases age 30-49; 32.3% fewergay or bisexual male patients; and 1.8% more cases in the 'no known risk group' category and 11.1% fewer and 10.6% more diagnoses of Kaposi's Sarcoma and Pneumocystis carinii Pneumonia only respectively.

Implications of these results are discussed in light of recently described epidemilogy of all AIDS cases among Black persons ,native and non-native, in the U.S.

THP.88 HIV infections in rural areas of West Africa(Guinea Bissau)

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In November 1985,sera from 98 individuals has been taken in two rural areas in Guinea Bissau,used for trypanosomiasis studies,and stored until now.In the first area,Biombo,we studied 48 sera from the inhabitants of village("tabanca")Cupedo,50 km from the capital Bissau.In the second area,S.Domingos,in the north of the country,a few kilometres from the border of Senegal we studied 50 sera from the inhabitants of two villages,26 from "tabanca" Djugul and 24 from "tabanca" Colage.

We used the ELISA and the Western blot both to HIV type 1 and HIV type 2,and the IFAT to HIV type 2 in the 98 sera.

HIV 1 antibodies were detected in 6 of 48 inhabitants of Cupedo(12.5%),5 males and 1 female;in Djugul HIV 1 antibodies was detected in 1 female over 26 inhabitants(3.8%), and in Colage in 1 female over 24 inhabitants(4.2%).

In Cupedo we have finded 5 positive cases over 48(10.4%)for HIV 2,1 male and 4 females; in Djugul HIV 2 antibodies were detected in 7 individuals over 26(26.9%),1 male and 6 females,and in Colage HIV 2 antibodies was detected in 1 female over 24 individuals(4.2%).

These findings indicates that HIV 1 and HIV 2 may be endemic in certain West Africa countries.

THP.89 Acute Infection by H.I.V. in Drug Addicts.

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The diagnosis was established in 17 out of 365 DA for onset of mononucleosis-like syndrome and of H.I.V.-Ab seroconversion. The duration of the acute illness ranged from 15 to 66 days. The incubation period was 2-3 months in 4 DA with chain transmission (syringe sharing among them and subsequent infection during this phase), but unknown in the other 13 for previous repeatedly sharing. Seroconversion occurred about 1 month after disease onset.

The acute phase was characterized, when compared with control seronegative DA, by an increase of WBC ($\bar{x}$: 9350), lymphocytes (not as relative count!) and especially of CD8 ($\bar{x}$: 1626, 44%) and by a moderate reduction of CD4. This picture might stand for the immune response to the infection, particularly characterized by the increase of the cytotoxic portion of CD8, as it happens during other viral infections (CMV, EBV, HSV). On the other hand, 3 patients did not show this picture: neither WBC, nor lymphocytes, nor CD8 ($\bar{x}$: 935) were increased, whereas CD4 were even more reduced. They had all a severe post-infectious chronic active hepatitis and thus likely a pre-existent alteration of the immune system (IS), which might have prevented CD8 from their cytotoxic response.

Consequently the CD8 increase lack might suggest a functional failure of the IS, particularly of CD4, and predict an unfavorable evolution. As a matter of fact these 3 patients showed later on a CD4 fall, which was considerably stronger, if compared with that of the other 13.

THP.90 Comparison of a novel RIPA/SDS-PAGE to immunoblotting and virusculture

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A RIPA using ^{125}I-labeled HIV antigens, enriched for gp120/41^{env} (GRIPA) was compared to immunoblotting (IB) for sensitivity and specificity for HIV antibodies. Sequential sera from 8 seroconverted homosexuals were tested. In all cases antibodies to gp120/41 and more prominent to p24, were found. In two cases these antibodies were detected earlier than by IB. It appeared that the GRIPA was 10 times more sensitive for anti-p24 in serial dilutions of eight serumsamples, while the detection of anti-gp120/41 was similar in IB. In one of 78 randomly chosen EIA-negative sera from homosexuals, antibodies to p24 could be detected. This early seroconversion was confirmed three months later by IB. The specificity of the GRIPA was demonstrated by analyzing 10 EIA- negative sera from homosexuals collected during two years. All sera were found negative in the GRIPA and the persons revealed no signs of HIV infection. Six blood donors reactive for p24 in IB for two years but negative in the GRIPA, were also studied. Virusculture was attempted with six seropositive asymptomatics as a positive control group. The six p24 IB positive persons were culture negative, while a 100% correlation existed between GRIPA and virusculture. It is concluded that reactivity in IB to p24 may be false positive, whereas reactivity in the GRIPA to p24 only is highly suspicious. This feature in addition to the high sensitivity for gp120/41 makes the GRIPA an useful confirmatory assay in sera with conflicting results in other HIV antibody assays.

THP.91 Mothers of Infants With HIV Infection: Outcome of Subsequent Pregnancies

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One hundred and thirty-four cases of perinatal HIV infection have been identified in South Florida between January 1981 and December 1986. These infants were born to 109 HIV infected women. Risk factors identified include drug abuse in 22% of the mothers and the remainder had no identifiable risk factor other than heterosexual contact with an infected person. All but one of the mothers were clinically well at the time of delivery of their first infant with HIV infection emphasizing that the infected child is frequently the first member of a household to be identified as infected. Subsequent to the birth of the index pediatric case 33 (30%) of the 109 women have developed ARC or AIDS and 18 (17%) have died. Twenty-five women have had 42 subsequent infants after the index case. Two women and their 3 children have been lost to follow-up. The remaining 23 women and their infants have been followed prospectively. Length of follow-up families ranges from 6 months to 5 years with a mean of 32 months. Fifteen women have more than 1 infected child. Of the subsequent siblings, 21 (54%) are infected and 18 (46%) are not infected. Of the 21 infected siblings 12 have died (60%). None of the unaffected siblings have died. Family patterns of disease include families that have 2 children with encephalopathy, one family that has 3 children with wasting syndrome and 1 family that has 2 children with severe lymphoid interstitial pneumonia. Infants born to HIV infected women who have delivered a previous HIV infected infant are themselves at significant risk for infection. These results may reflect a special population of women and further studies are required to determine also the risk of having an infected child in women without previously infected children.

THP.92 Heterosexual Transmission of Human Immunodeficiency virus (HIV): Relationship of Sexual Practices to Seroconversion.

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To evaluate the efficacy and potential role of condom use in the prevention of heterosexual transmission of HIV, spouses of patients with AIDS and AIDS-related complex were evaluated. Evaluation included a medical history, physical examination, standardized interview, and blood tests. All spouses were counseled and followed every 4 months. Forty-seven seronegative spouses were studied. Twelve were men and 35 were women. None had risk factors for HIV infection. The median length of followup was 18 months. Seventeen (36%) developed antibody to HIV; 4 (33%) were men and 13 (37%) were women. The relationship of sexual practices after enrollment to the development of antibody to HIV is shown below.

	number	HIV antibody		percent
		positive	negative	converted
abstinence	12	0	17	0%
condom use	18	3	15	17%
no condom use	17	14	3	82%

The frequency of sexual intercourse and types of sexual activity were not different for spouses using condoms compared to those not using them. In evaluating couples who used condoms, breakage, improper use and fellatio without condoms was not uncommon. Although condom use appeared to decrease the rate of HIV transmission, seroconversion occurred. These data suggest that condom use may not afford complete protection against the heterosexual transmission of HIV.

THP.93 Prevalence of HIV-1 and HIV-2 antibodies in a selected Malawian population

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Screening for HIV infections in Malawi was began in 1986 to evaluate the prevalence of HIV-1 and HIV-2 in this part of Africa. 96 antenatal mothers, 265 female prostitutes and 32 male prisoners were screened with a commercially available ELISA for HIV-1 and an ELISA prepared in our laboratory for HIV-2 using LAV-2, kindly provided by L. Montagnier. Positive reaction in the ELISA tests were confirmed by immunofluorescence and immunoblot. In addition, the presence of markers of infection with other sexually transmitted agents, i.e. hepatitis B virus (HBV) and treponema pallidum (TPA) was determined.

The results are given in the table as positive/number tested (percent).

markers for	HIV-1	HBV	TPA
antenatal mothers	4/96 (4%)	67/96 (70%)	26/96 (27%)
female prostitutes	148/265 (56%)	219/265 (83%)	143/265 (54%)
male prisoners	10/32 (31%)	18/32 (56%)	11/32 (24%)

50 of the sera of prostitutes positive for anti-HIV-1 also were screened for anti-HIV-2. Antibodies specific for HIV-2 antigens were not detected. However, crossreactions of anti-HIV-1 with HIV-2 antigens were observed, particularly reactions of anti-HIV-1-p24 core with HIV-2-p27. The results show that infections with HIV, HBV and TPA are common in this part of Africa; but it is not justified to calculate from only 393 individuals investigated so far the prevalence of anti-HIV in the 7 million inhabitants of Malawi. Ongoing studies should clarify this further.

THP.94 Berlin prospective Study on 35 HIV (human immunodeficiency virus) Antibody-Positive Newborns

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The presence of HIV-IgG-antibodies (AB) in newborns (NB) of HIV-AB-positive mothers does not provide conclusive evidence of an actual infection with the virus. This is determinable only by longterm observation of the patients, concerned in accordance with immunological, virological and clinical criteria.

Consequently, since July 1985, all NB of HIV-AB-positive mothers are being kept under close observation at the Berlin University Children' Hospital and 35 newborns have so far been icluded in the study.

During an observation period of now over 18 months, none of the children have as yet contracted AIDS. A slight neurological abnormality was apparent in 2 children.One child who suffered a bacterial meningitis at 11 months of age had become seronegative at 6 months of age. The HI-virus was identified in CSF at the time of meningitis despite further seronegativeness.

One child whose clinical course was extraordinary (weight stagnation, recurrences of candidiasis) died at 7 months(sudden infant death).

As expected, 15 children whose virus culture was negative, became seronegative at between 3 to 7 months, however also 4 children with a positive virus culture became seronegative.

The results clearly show that AB-Screening is not a sufficient method of course control, but that longterm observation is essential for accurate classification of HIV-AB-positive newborn children.

THP.95 The Geographic Distribution of Human Immunodeficiency Virus (HIV) Antibodies in Parenteral Drug Abusers (PDAs)

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Opioid dependence treatment programs in 5 regions of the US collaborated in a study aimed at monitoring trends in seroprevalence of HIV antibodies. After informed consent, 1,650 PDAs volunteered to provide blood specimens and data on health history and patterns of drug use. While this sample cannot purport to be representative of PDAs in the region, nor even of PDAs in treatment within the region, the wide disparities in HIV seroprevalence in the face of similarities in drug using behavior have important implications for prevention. In the New York area (Harlem, Brooklyn), 61% of samples (N=280) obtained in late 1986 were positive, up from 50% of samples (N=585) from the same program taken in early 1984. In Baltimore, 29% of samples (N=184) representing 11 programs were positive. Significant sex and ethnic group differences were apparent. In contrast, samples from programs distant from the Northeast corridor had far lower rates: San Antonio, 2% (N=106); Tampa, 0%; Southern California, 1.5% (N=413, with samples from programs from Fresno to San Diego). Contrary to expectations, there was no corresponding difference in lifetime needle sharing experiences, which ranged from a low of 70% in New York to 99% in San Antonio. Because needle sharing is practiced by PDAs in areas where seroprevalence is still relatively low, these areas are vulnerable to the same catastrophic spread seen in the Northeast. But a window of opportunity where prompt, vigorous, and aggressive efforts at prevention could have major impact.

THP.96 IgM Antibodies to HIV in Sera from HIV-Infected Homosexual Men in Montreal

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Sequential sera from 163 homosexual men, infected with HIV confirmed by IgG seropositivity, were assayed for IgM antibodies to HIV. They were selected from a private practice, and consisted of 28 men who IgG-seroconverted; 12 men who reverted from IgG-seropositive to negative; and 123 men who were persistently IgG-seropositive. 133 men were asymptomatic at the time of serum collection; 30 men had ARC; and 10 later developed AIDS. Duration between serum samples was 9.8 months ± 4.6 (SD). IgM antibodies were detected by IgM-ELISA after rheumatoid factor adsorption. Cut-off for this assay was 7 SD above the mean of IgM-seronegative controls. Specificity of IgM antibodies was confirmed by IgM-Western blotting.

IgM antibodies were detected in the sera of 14 men, or 8.6% of this cohort: 2 of 28 men who IgG-seroconverted, including one man who had IgM antibodies when IgG antibodies were undetectable; none of 12 men who IgG-seroreverted; and 12 of 123 men who were persistently IgG-seropositive, including 3 men who developed IgM antibodies when already IgG-seropositive and 6 men who remained persistently IgM-seropositive. 8% of asymptomatic men, 10% of men with ARC and 10% of men who subsequently developed AIDS had IgM antibodies detectable in their sera. Western blotting showed IgM antibodies reacted with recognized HIV antigens but with a different pattern than that of IgG antibodies.

These data show that IgM antibodies to HIV are detectable at low frequency in sera of HIV-infected homosexual men, and appear unrelated to IgG antibody responses or to HIV disease manifestations.

THP.97 High Prevalence of Serum Antibodies to HTLV-III p66/p51. A.L. DeVICO*, F. diMARZO VERONESE*, R.C. GALLO**, M.G. SARNGADHARAN*, *Bionetics Research, Inc., Rockville, MD; **Lab. of Tumor Cell Biology, NCI, Bethesda, MD.

The reverse transcriptase of HTLV-III is detected in immunoblot assays as a pair of 66 kD and 51 kD proteins (p66/p51). These proteins share a common NH_2 terminal amino acid sequence; whether both proteins are enzymatically active has not been determined. A preliminary study indicated a high seroprevalence of RT antibodies in HTLV-III antibody-positive individuals tested by the viral immunoblot technique. Further, some individuals had serum antibody reactivity with only p66. To more accurately determine the frequency of serum antibody reactivity with RT, the results of 700 immunoblot assays of HTLV-III antibody-positive sera were examined. Seropositivity was determined by reactivity with gp41, p24 or both. Of the sera selected, 79% were positive for antibodies to p66/p51. Such immunogenicity for RT has not been demonstrated for any noncytopathic mammalian retroviruses including HTLV-I and -II. The seroprevalence of reactivity with RT seems to vary with the stage of the disease. Out of the 700 sera 360 for which a diagnosis was available were divided into 4 groups consisting of asymptomatic individuals at high risk, ARC patients, AIDS patients and AIDS patients with Kaposi sarcoma. Seroreactivity to p66/p51 was found in 75%, 85%, 77%, and 78% of the individuals in each group, respectively. Serum from the individuals with antibody reactivity to only p66 were retested in an immunoblot assay using purified enzyme bound to nitrocellulose. All of the individuals tested had serum antibody reactivity with p51 but the level of reactivity remained much lower than that for p66.

THP.98 Recreational Drugs and HIV Infection: Relationship to Risk of Infection and Immune Deficiency. Cladd E. Stevens, Patricia E. Taylor, Santiago Rodriguez and Pablo Rubinstein. New York Blood Center, 310 East 67th Street, New York, New York, U.S.A.

In early 1984 the Laboratories of Epidemiology and Immunogenetics at the New York Blood Center began a prospective study of the acquired immune deficiency syndrome (AIDS) in a cohort of 850 homosexually active men in New York City. At the time of entry into the project in 1984, each participant completed a self-administered questionnaire which contained quantitative questions regarding use of 21 recreational drugs or categories of drugs, including amyl and butyl nitrite. Participants have returned every four months at which time an interim history is obtained and cellular immune function is assessed.

At the time of entry 42.3% of the men were anti-HIV positive. Anti-HIV prevalence at that time correlated with the use of each of the 21 recreational drugs for which we solicited information. However, recreational drug use also correlated with sexual activity, including numbers of sex partners and frequency of high risk sex practices, factors which were the strongest predicters of anti-HIV positivity. No consistent association between history of use of any drug and defects in cell mediated immunity detected among anti-HIV positive men at entry was observed. Over the past two-and-a-half years, 47 of the participants have been diagnosed as having AIDS. No association was found among the anti-HIV positive men between history of drug use and the subsequent development of AIDS.

These preliminary data suggest that the relationship between recreational drug use and the risk of HIV infection is secondary to the association with sexual activity and that drug use had no subsequent influence on the development of defective CMI or AIDS.

THP.99 Correlation of HIV Isolation Rate and Stage of Infection. RR REDFIELD, DC WRIGHT, NC KHAN, DS BURKE, WRAIR, Washington, DC.

HIV infection causes a spectrum of disease which can be placed in a working framework of progressive stages of viral-induced immune dysfunction as proposed by the Walter Reed Staging Classification. We investigated the ability to isolate HIV from perpheral blood mononuclear cells (PBMC) of patients with different stages of HIV infection. All retroviral cultures were performed and interpreted blindly with respect to clinical status. Cultures were performed using patient PBMC obtained by Ficol hypaque separation from 30 ml of whole heparized blood which were co cultivated with PHA-stimulated normal donor PBMC. Cultures were monitored for viral production by both reverse transcriptase and HIV antigen-specific assays for 30 days. Results are summarized in tables below.

TABLE 1

WR STAGE	N	#POS	%POS
1	3	0	0%
2	34	9	26%
3	3	1	33%
4	3	1	33%
5	6	5	83%
6	5	4	80%
TOTAL	54	20	37%

TABLE 2

T4#	N	#POS	%POS
>800	8	1	13%
600-799	16	2	13%
400-599	13	6	46%
200-399	6	3	50%
100-199	5	3	60%
<100	6	5	83%
TOTAL	54	20	37%

These data demonstrate a significant correlation ($P<0.001$) of the ability to isolate HIV from PMBC with (1) Walter Reed stage and (2) T-helper cell number. The biological explanation of these differences is currently under investigation.

THP.100 Serial T Cell Phenotypes in Homosexual Men Who Did or Did Not Progress to AIDS.

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A cohort of 75 HIV-antibody-positive homosexual men with chronic lymphadenopathy has been studied serially for the last 3-4 years in Atlanta. As of January 1987, 21 have developed acquired immunodeficiency syndrome (AIDS). To determine whether those who developed AIDS are immunologically different from those who did not develop AIDS, we retrospectively examined the distribution and number of subpopulations of CD4 and CD8 lymphocytes in 5 men who progressed to AIDS and 10 men who did not over the last 3-4 years. Two-color immunofluorescence studies were done with combinations of monoclonal antibodies to detect functionally defined subpopulations of CD4 cells (helper-inducer [$CD4^+4B4^+$], suppressor-inducer [$CD4^+2H4^+$], and "activated" [$CD4^+HLA\text{-}DR^+$]), CD8 cells (cytotoxic [$CD8^+Leu15^-$], suppressor [bright $CD8^+Leu15^+$], "reactive" [$CD8^+Leu7^+$], and "activated" [$CD8^+HLA\text{-}DR^+$]), as well as phenotypes associated with natural killer (NK) activity (dull $CD8^+Leu15^+$ and $Leu7^-Leu11^+$). CD4 cells declined more rapidly in patients who progressed to AIDS, than in those who did not. None of the CD4 subset, CD8 subset, or NK-associated subset enumerations clearly distinguished progressors from nonprogressors. However, each progressor had a unique phenotype change that progressed with time, such as a severe depression in $Leu11^+$ cells, increases in $CD8^+HLA\text{-}DR^+$ cells, increases in the proportion of CD3 cells that are $Leu7^+$, and the proportion of CD4 cells that are $4B4^+$ or $2H4^+$. These changes were seen in only 2 of the 10 nonprogressors; the remaining 8 had stable phenotypes. These unique changes may reflect a failing immune system.

THP.101 Abnormal Lymphokine Activated Killer Cell (LAK) Induction in Peripheral Blood Mononuclear Cells (PBMC) in Patients Infected with the Human Immunodeficiency Virus (HIV)

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The ability to generate LAK cells from the PBMC of asymptomatic homosexual males (AHM) with serologic evidence of HIV infection (n=25) was evaluated. HIV infection was determined by the presence of antibodies (Ab) to HIV proteins or by the presence of HIV core antigen (Ag). LAK cell generation was normal in HIV Ab^+ Ag^- AHM (mean % cytotoxicity = 46±13 compared to a control group of seronegative AHM where mean % cytotoxicity = 45±16). In contrast, the LAK cell induction was significantly impaired in AHM who were HIV Ab^+ Ag^+ (mean % cytotoxicity = 16±9, $p<0.01$ compared to controls). The mechanism for suppressed LAK induction was evaluated and found to be due to an indomethacin (indo) sensitive suppressor function. Thus, the addition of indo to cultures of cells from Ab^+ Ag^+ AHM restored their LAK function to control levels (mean % cytotoxicity = 46±9). The presence of this indomethacin sensitive suppressor in Ab^+ Ag^+ AHM was also documented in mitogen stimulated blastogenesis and IL-2 production assays and was correlated with significant depression of monocyte HLA-DR expression (32±11% $LeuM3^+$ $HLA\text{-}DR^+$ monocytes vs 82±15% $LeuM3^+$ $HLA\text{-}DR^+$ monocytes in controls, $p<0.01$). The deficits in LAK cell induction and mitogen stimulated blastogenesis which were observed in the group of patients who were Ab^+ Ag^+ were associated with HIV recovery from the monocytes of these individuals. These findings have important implications for our understanding of the pathogenesis of HIV infection and may point the way to new methods for therapeutic intervention.

THP.102 Immune Response and Challenge of Chimpanzees Immunized with a gp41 Synthetic Peptide. G.R. DREESMAN*, T.C. CHANH*, P. KANDA*, J.W. EICHBERG*, R.C. KENNEDY*, J.S. ALLEN**, et al. *Southwest Foundation for Biomedical Research, San Antonio, Texas, **Harvard School of Public Health, Boston, Massachusets.

Two chimpanzees were immunized with a synthetic peptide containing amino acid residue 735-752 of gp41 transmembrane glycoprotein of HIV coupled to KLH. A third animal was inoculated with an unrelated peptide KLH conjugate. Both animals immunized with the gp41 peptide produced an antibody response which reacted with native gp41 and gp160. The three animals were challenged with HIV-NY5 isolate after 4 injections of immunogen and have been studied for 24 weeks post challenge for antibody response and virus isolation. Antibody response to viral protein p24 and gp120 was similar between the control animal and the first peptide immunized animal. However, antibody to these proteins were delayed approximately 4 - 6 weeks in the second animal. Virus isolation studies are in progress.

THP.103 Pediatric HIV infections in HIV-ELISA negative individuals: a report of 10 cases.

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The presence of HIV specific antibody has been used to document HIV infection in patients. Both ELISA and immunofluorescence (IFA) have been used for screening. Rarely, sera considered negative by HIV-ELISA assay is found to be reactive with virus specific bands on Western Blot assay (WB). Although these assays can produce false positive results in children below 1 year of age due to the presence of transplacentally derived maternal HIV specific IgG, we have found that false negative responses may be more common than previously suspected. We have identified about 90 children infected with HIV. Ten of these were considered to be HIV-ELISA negative but found to possess HIV antigen in their plasma, as measured by an antigen capture ELISA assay, with estimated viral antigen concentrations of 13 to 756 pg/ml. Five of the ten have died of AIDS. Nine of the ten were born to drug abusing mothers. Five of the mothers had HIV-ELISA antibody tests performed on their sera and all were positive. Nine of the children had decreased helper T cells. IFA performed on 6 of the sera was negative. WB assays performed on 5 of the sera were negative. Four of the children had supporting evidence of HIV infection as determined by the presence of anti p121 antibody found with a commercial assay which employs recombinant antigen (ENVACOR). Since HIV infected infants have impaired primary antibody responses to other antigens, a comparably impaired response to HIV antigens may result in negative antibody assays. HIV antigen measurement appears to be an important tool to identify these infants.

THP.104 Viruses of Human Immunodeficiency Virus Family Induce Expression of Class II Major Histocompatibility Complex Structures on Infected Target Cells In Vitro

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The human immunodeficiency virus (HIV) and the closely related simian immunodeficiency virus (SIV) induce profound immune dysfunction in primate species. We have now shown that cell populations infected in vitro with these viruses exhibit increases in major histocompatibility complex (MHC) class II antigen expression. Cell lines chronically infected with both the monkey and human viruses express substantially more MHC class II but not more lineage-restricted or activation antigens on their membranes than do uninfected cell lines. No serologic cross-reaction was observed between MHC class II and viral specific antigens. MHC class II induction does not appear to be mediated through the production by infected cells of a soluble factor such as gamma interferon. Studies of the kinetics of antigen expression by cell lines following SIV-infection indicate that induction of MHC class II structures is a late event. Immunoelectronmicroscopy revealed that MHC class II antigen is expressed not only on the surface of the SIV-infected cells, but also on the envelope of virus particles derived from those cells. MHC antigen expression on virus infected cells and expression of those determinants by the virus may play a role in the pathogenesis of AIDS and the autoimmune abnormalities obaerved in HIV infected individuals.

THP.105 CORRELATION OF DELAYED HYPERSENSITIVITY SKIN TESTING AND ABSOLUTE T4 NUMBER AND T4/T8 RATIO. D.L. Birx, J. Rhoads, L. Smith, C. Wright, D. Burke, R. Redfield. Walter Reed Army Medical Center and Walter Reed Institute of Research, Washington, D.C. USA.

We have evaluated 400 consecutive HIV ELISA and Western Blot confirmed seropositive patients who presented for evaluation and staging. Each individual underwent anergy screening with simultaneous, absolute lymphocyte and T4 counts, and T4/T8 ratio. The anergy panel consisted of PPD 5TU, two concentration of tetanus toxiod (TT) and candida albicans (CA) 0.1Lf, 1.0 Lf and 1:10 w/v 1:100 w/v respectively, mumps, and trichophyton. 5x5 mm induration was considered positive at 48 hrs. Complete data is presented on 337 patients in tabular form.

skin test results	(n)	T4 (#/mm3)±SDx2	T4/T8 ratio ± SDx2
1. anergy	45	172 ± 152	.27 ± .20
2. TT (1Lf)CA(1:10 w/v)	39	412 ± 237	.56 ± .39
3. 1/5	61	481 ± 299	.64 ± .41
4. 2/5	77	530 ± 250	.64 ± .29
5. 3/5 TT (0.1 Lf)	71	637 ± 263	.84 ± .46
6. 4/5 CA (1:100/v)	39	614 ± 374	.75 ± .46
7. 5/5	5	550 ± 160	.67 ± .31

There is statistical significance between the T4 counts and ratios of those who are anergic and all other catogories $p < 0.01$, as well as, those who are only positive to the higher concentration of TT and CA (# 2 vs # 5) $p < 0.05$. A trend can be seen between the number of positive skin test responses and T4 counts and T4/T8 ratios. All individuals are being followed for correlation with disease progression.

THP.106 Anti Nucleo-Capsid antibodies and S-HIV antigenemia: correlations with blood T4 cell counts and clinical status.
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Serum HIV antigen concentration was measured by immune capture where untreated serum is incubated with solid phase human anti-HIV IgG and further reacted with rabbit IgG recognizing HIV (mainly) core antigen (P24).Anti-Nucleo-Capsid antibody assay used recombinant (mainly) P24 protein (solid phase) and competing human anti-HIV IgG. Inhibition > 85% that of anti-HIV IgG arbitrarily defined a high (affinity/titers) NCA antibody specimen (H-NCA- Ab).

A reciprocal distribution between S-HIV-Ag and H-NCA-Ab was found: 71 S-HIV-Ag positive among 98 without H-NCA-Ab compared with 6/57 with H-NCA- Ab (80% versus 11.5%). S-HIV-Ag was detected in 41/72 patients with T4 <200/ul and 26/74 with T4>700 while H-NCA-Ab were detected in 16/82 and 53/90, respectively. Among patients without H-NCA-Ab, S-HIV-Ag distribution was independent of T4 counts. These results suggest that S-HIV-Ag may contribute to declining anti-Core antibody (in our serially tested patients) but that it is not a main factor in the pathogenesis of T4 lymphopenia.

In contrast, 12/18 Kaposi patients with T4>200 had detectable S- HIV-Ag compared with 36/111 non-Kaposi patients. Conversely H-NCA-Ab were found in 3/20 Kaposi patients vs 102/195 non Kaposi(15% vs 52%).Soluble viral products could play an active part in pathogenesis of Kaposi independently of the process leading to T4 lymphopenia. Accordingly, H-NCA-Ab would act as anti-kaposigenic factor.

THP.107 The Thymus-AIDS Connection: HIV p17 Protein Contains an Epitope Immunoreactive with Antisera to Thymosin α_1 and HGP-30, a Synthetic gag Peptide Analogue
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The p17 protein of Human Immunodeficiency Virus (HIV) contains an epitope which has a 44-50% homology with an 18 amino acid region of thymosin α_1 ($T\alpha_1$), a thymic hormone. Using solid phase peptide synthesis we have synthesized a 30 amino acid analogue of this p17 epitope which we have termed HGP-30 (HIV p17 gag synthetic peptide — 30 amino acids). Using high performance liquid chromatography, radioimmunoassay (RIA), and Western blot analysis, the presence of this immunoreactive epitope in a 17,000 dalton protein from an HTLV-IIIB viral extract has been identified. No significant immunoreactivity was found in a number of other retroviral extracts including those obtained from feline, bovine, simian and murine retroviruses. These results, coupled with our previous studies demonstrating immunoreactive but non-authentic $T\alpha_1$-like material in serum from viral infected individuals at risk for or with frank AIDS confirms our hypothesis of a Thymus-AIDS connection. The demonstration that an antisera to HGP-30 cross-reacts with HGP-30 but not with $T\alpha_1$, and identifies the same protein as a p17 monoclonal antibody suggest that an ELISA or RIA can be developed that would be diagnostic for the presence of antibodies or antigens in individuals that are seropositive for the AIDS virus.
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THP.108 Intrathecal Synthesis of IgG Oligoclonal Bands with Specific Activity Against Human Immundeficiency Virus (HIV) in AIDS Patients with Encephalopathy
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Involvement of the nervous system, including encephalopathy, is increasingly recognized as a frequent finding in AIDS. Evidence is accumulating that the HIV virus not only attacks the immune system but also affects the central and peripheral nervous system. The pathogenesis of the neurological damage however is very poorly understood. It has been demonstrated that HIV antigen and specific antibodies can be found in cerebrospinal fluid (CSF) with and without signs of encephalopathy. Usually encephalopathy is accompanied by intrathecal synthesis of IgG as demonstrated by quantitative indices of IgG and appearance of oligoclonal IgG bands in CSF. Our studies using isoelectric focusing of serum and CSF from patients with AIDS-related encephalopathy confirmed the presence of oligoclonal IgG banding. Some bands were common to serum and CSF and others present only in CSF. Using an immunoblot technique employing HIV precoated nitrocellulose paper, we have also demonstrated the presence of several HIV specific IgG bands in the sera and CSF of patients with AIDS-related encephalopathy. Most HIV antibody bands are present in both serum and CSF; some are present exclusively in the serum or CSF. Negative controls included sera from patients with gammopathy and HIV antibody positive samples blotted to nitrocellulose paper precoated with control, non-infected H-9 cell culture preparations. These findings demonstrate that HIV antibodies develop in the CNS and specific B-lymphocyte clones are stimulated to produce monoclonal IgG antibodies to HIV in the CNS. These findings strongly support a direct causative role of HIV in AIDS-related encephalopathy.

THP.109 Differential Susceptibility of $CD4^+$ T Lymphocyte Clones to HIV Infection
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It has been reported that only 10-15% of normal circulating lymphocytes will avidly bind and support replication of HIV in vitro. To evaluate the differential susceptibility of T4 cells to HIV infection, a panel of 10 $CD4^+$ CDB^-, IL-2-dependent alloreactive clones were generated from a healthy HIV seronegative volunteer. The clones were infected with HIV-1 at a multiplicity of infection of 0.1 and 1.0. HIV infection was monitored for 21 days by examination of cultures for cytopathic effects and by assay of supernatants for reverse transcriptase (RT). Eight of 10 clones showed no evidence of HIV infection.

Two clones, one supporting HIV replication (CL62) and another showing no evidence of infection (CL40), were used for subsequent studies. Prior to exposure to HIV, both clones expressed similar levels of CD4, HLA-DR, and TAC antigens and showed comparable levels of alloantigen specific-proliferation in a 4 hour ^{3}H-TdR incorporation assay. Fourteen days following HIV infection of CL62, peak RT activity was measured. Ten to 50% of these cells were infected as detected by in situ hybridization for HIV RNA. No viable cells were present in these infected cultures after 30 days. In contrast, CL4D produced no detectable RT activity or HIV proteins in an antigen capture assay and continued to proliferate and expand 2-3 fold over the same time interval. However. 0.1% of CL40 cells contained HIV RNA by in situ hybridization and virus from the cell free-supernatants of these cultures could be passaged to normal PHA-stimulated lymphocytes. Differential susceptibility to infection of normal T4 cells with HIV may be determined by cellular factors exclusive of specific receptor expression (CD4) and cellular activation.

THP.110 Abrogation of Mitogen Response of Normal Lymphocytes by Anti-lymphocyte Antibody Positive Sera of AIDS and ARC Patients.
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We have previously reported the presence of elevated levels of antilymphocyte antibodies (ALA) in the sera of patients with acquired immune deficiency syndrome (AIDS) and AIDS related complex (ARC). In addition we have demonstrated that ALA are statistically linked to disease progression. In order to determine whether sera containing elevated levels of ALA might affect lymphocyte function we have examined their effect on the mitogen response of normal peripheral blood lymphocytes. Whole blood from healthy volunteers was cultured in RPMI 1640 in the presence of mitogenic levels of Phytohemagglutinin (PHA). Cultures were treated with ALA positive AIDS and ARC sera as well as ALA negative control sera. At various intervals cells were harvested and hypotonically lysed in the presence of Propidium Iodide. After treatment with Ribonuclease the relative level of lymphocyte stimulation was determined by flow cytometric measurement of the proliferating cell compartment. The mitogenic effect of PHA on normal lymphocytes was substantially reduced by treatment with ALA positive sera. Reductions varied from 40 to 95%. Treatment with ALA negative sera failed to affect mitogen response.

THP.111 IDENTIFICATION AND CHACTERIZATION OF AN IMMUNODOMINANT EPITOPE ON THE GP41 HIV ENVELOPE PROTEIN. R. WISNIEWOLSKI, P. D. CHEN, J.G. WANG, W.WALTERS AND C.Y.WANG. United Biomedical, Inc. Lake Success, N.Y.

We have previously identified a peptide 21 residues in length corresponding to a highly antigenic segment of HIV gp41 envelope protein(PNAS 83: 6159,1986) and included this peptide in a synthetic mixture as the solid phase immunoadsorbent for the detection of anti-HIV in individuals with HIV infection.

When this peptide was conjugated to a protein carrier (HSA) and used as an immunogen, high level of antibodies directed against this peptide was found to cross-react with the whole HIV lysate.

When attenuated HIV was used as the immunogen, after fusion with NS-1 myeloma cells, a high frequency (80%) of monoclonal anti-HIV antibodies screened out by Enzyme Immunoassay on HIV lysate fixed plates were found to be negative by Western Blot (WB) analysis. These EIA-positive WB-negative HIV antibodies, frequently discarded by investigators due to their seemingly low affinity nature, were found to react specifically with the 21mer antigenic peptide.

Further analysis of these monoclonal anti-HIV gp41 antibodies, developed through immunization with either the peptide-conjugate or the HIV lysate, with peptide analogs of this 21mer has enabled us to precisely delineate each of their corresponding epitopes at a single amino acid level. Although no inhibition of HIV binding to CEM-T cells were observed with these antibodies, preferential recognition of this gp41 epitope may indicate an important functional role of this region in the initiation of an immune response through antigen presentation or T cell activation.

THP.112 UV-HIV Immunosuppression of Mitogen Responses by Normal PBL Can Occur in the Absence of Cytopathology

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Decrease in T4 cells cannot account for the full extent of the immune defects seen in AIDS or ARC patients. Immune defects can be demonstrated in seropositive patients with T helper/T suppressor cell (T4/T8) ratios in the normal range. Normal peripheral blood lymphocytes (PBL) incubated with PHA and uv-inactivated HIV (UV-HIV) were examined with specific monoclonal antibodies to various T cell subsets by flow cytometry. Three out of 7 individuals tested exhibited a 25-30% decrease in Leu 3a positive cells, and a marked decrease in T4/T8 ratios over a 7 day incubation period. This decrease was accompanied by a varied but consistent increase in Leu 2a positive cells. Preactivation of PBL's with PHA alone and subsequent exposure to UV-HIV in the presence of PHA exhibited inconsistent Leu 3a killing and T4/T8 ratio changes in susceptible individuals tested in repeated experiments. The effects of UV-HIV on the proliferation of normal PBL's cultured in the presence of PHA were studied. UV-HIV, intact or detergent solublized, suppressed PHA stimulated proliferation of donor PBL's over a broad range of PHA concentration even in the absence of cell killing. This effect was dependent upon the quantity of UV-HIV or solublized UV-HIV. The elaboration of a putative suppressor factor from cultures of UV-HIV treated PBL's in the presence of PHA will be discussed. Demonstration of marked immunosuppression in the absence of Leu 3a killing and changes in T4/T8 cell ratio, indicates the possibility that the two phenomena may be mediated by two different proteins or the same protein may serve several functions.

THP.113 Patterns of Lymphocyte Subset Alterations in SIV/Delta Infected Rhesus Monkeys.

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Simian Immunodeficiency Virus (SIV/Delta) infection of rhesus monkeys induces immunodeficiency, opportunistic infections (OI) and death. OI manifestation postinoculation varies from 2 to 21 months. Studies of lymphocyte subsets by staining with monoclonal antibodies revealed two patterns of alterations in SIV/Delta infected monkeys, one of which may be prognostic of imminent OI. Monkeys dying with OI by 8 months after SIV/Delta inoculation developed increased percentages of T-11$^+$ (erythrocyte receptor) and Leu 2a$^+$ (suppressor/cytotoxic) cells. Depressed helper/suppressor (H/S) ratios resulted from the increase in the percentage of Leu 2a$^+$ cells. Although these animals had normal percentages of Leu 3a$^+$ (helper/inducer) cells, the percentages of these cells staining with 4B4 was decreased, indicating a defect in a more restricted helper/inducer subset. Five of the 7 inoculated monkeys which exhibited this pattern of subset alterations died within 8 months postinoculation, and 4 of the 5 monkeys which died also had progressive decreases in serum IgG concentrations. Monkeys which survived longer than 8 months developed decreased percentages of T-11$^+$ and Leu 3a$^+$ cells and increased percentages of B-1$^+$ cells. Depressed H/S ratios in this group resulted from the decrease in Leu 3a$^+$ cells. Although the percentage of Leu 3a$^+$ cells was depressed, the percentage of these cells staining with 4B4 was normal. All 6 inoculated monkeys which exhibited this pattern of subset alterations, including increased B-cell percentages, had progressive increases in serum IgG. One monkey in this group died 309 days postinoculation with a B-cell lymphoma. Seven of 9 monkeys tested had defective antibody responses to tetanus toxoid.

THP.114 Cellular Pathogenesis Induced by Human Immunodeficiency Virus

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We developed an in vitro system to study cytopathology induced by human immunodeficiency virus (HIV). We mixed an irradiated infected tumor cell line, H9, with peripheral blood mononuclear cells (PBMCs) and monitored the phenotype of lymphocytes. Rapid reduction of CD4$^+$ numbers occurred after 3-5 days in cultures containing irradiated H9/HIV. In contrast, no depletion occurred after incubation with K562 or uninfected H9 cells. Similarly, no depletion occurred after incubation of H9 cells with free virus in 5 days. Because we thought that antigen activation might play a role in the rapid CD4 depletion and because the quantity of free HIV may be different from that associated with H9/HIV cells, we examined the response to irradiated infected PBMCs. Allogeneic or autologous mixtures of PBMCs from person "A" or "B" were examined in cultures containing irradiated infected cells from person "B". In some A + B/HIV cultures, we noted dramatic depletion of cells within 5 days; in others only a modest reduction occurred. In B + B/HIV cultures, however, no reduction in CD4$^+$ numbers occurred after 5 days in culture although surface interleukin-2 receptor expression did occur. We, therefore, used PHA or CD3 Sepharose to provide a T cell receptor signal to the B + B/HIV cultures. We found that dramatic depletion of CD4$^+$ numbers occurred after PHA addition. CD3 also induced CD4 cellular depletion but to a lesser extent than did PHA. These results suggest that HIV must be associated with cells for optimal cytopathology and that lymphocyte activation, perhaps via allogeneic recognition, may be a primary mechanism involved in the acquisition of HIV in vivo. Supported by NIH grants AI22549 and AI21289.

THP.115 Antibodies to HIV are produced within the Central Nervous System of all subjects with all categories of HIV Infection

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Anti-HIV antibodies were found in the cerebrospinal fluid of all 41 subjects tested whose serum contained these antibodies. To ensure that locally produced antibody was being detected, a sensitive assay was used to demonstrate the integrity of the blood-brain barrier. Antibodies to ubiquitous adenovirus group antigens were sought, simultaneously, in CSF and serum. A lack of adenovirus antibodies in CSF of subjects seropositive for adenovirus was required before CSF anti-HIV antibodies could be considered to be produced within the central nervous system.

Of the forty-one subjects tested eight were asymptomatic, eight were clinically well but had significant lymphadenopathy, fourteen were immunodeficient and had constitutional symptoms (AIDS-related complex or ARC) and eleven had AIDS. Oligoclonal banding was detected in the CSF of sixteen subjects and a pleocytosis was present in twenty-four. Neither finding clustered with a particular stage of infection. It appears that serological evidence of HIV infection of T lymphocytes and of the central nervous system occurs simultaneously. All HIV infected subjects are at risk of developing primary neurological as well as immunological sequelae. Similarly, currently poorly understood resistance factors must protect both lymphocytes and nervous system tissue from damage by the HIV virus, as to date, the majority of infected subjects have not become immunodeficient or developed neurological disease.

THP.116 IMMUNOLOGICAL PARAMETERS IN HIV-INFECTED SPANIARDS:HIGH MONOCYTE NUMBERS IN PERSISTENT LYMPHADENOPATHY PATIENTS. Arnaiz-Villena A, Alcamí J, Regueiro JR,. Immunología,Hospital Primero Octubre, 28041 MADRID. SPAIN. The paleo-North African origin of the Spanish population makes it an interesting ethnic group for the study of AIDS in Caucasians.We have thus established the immunological status of the different stages of HIV infection in Spaniards. One hundred HIV$^+$ patients (as assessed by both Elisa and Western blot tests) were studied(81 drug addicts, 7 homosexual, 4 post-transfusional, 2 heterosexual transmissions,2 mother/child infected couples and 2 belonging to no obvious risk group) The following parameters were studied:peripheral blood mononuclear leukocytes (PBML) subpopulations (CD3,CD4,CD8,CD11 and CD20),serum immunoglobulins, in vitro proliferative response to phytohaemaglutinin (PHA), anti-CD3 and pokeweed, and anti-HIV proteins (p15,24,31,41,53,55,64 and 120) serum IgG antibodies. CDC clasification criteria were used:27 asymptomathic(AS),27 with persistent lymphadenopathy (LAP),26 with AIDS-related complex (RC) and 20 full-blown AIDS were observed.RESULTS:all patients had high polyclonal serum IgG levels and high CD8$^+$ PBML ($p < 0.05$) as compared to healthy controls.Interestingly,LAP patients showed high monocyte numbers (510 vs 331, $p < 0.05$) and CD11$^+$PBML (594 vs 282, $p < 0.001$) as compared to AS group, but both variables were back to normal values in RC and AIDS subsets; this may be of value for assessment of illness progress,and,in LAP individuals, dropping CD11$^+$PBML may indicate a poor prognosis.Compared to AS and LAP groups,RC and AIDS patients had lymphopenia ($p < 0.001$),low CD4$^+$PBML ($p < 0.001$), low CD4/CD8 ratio ($p < 0.001$) and low lymphoproliferative responses (PHA,$p < 0.001$; anti-CD3,$p < 0.01$). Lastly,compared to all other groups,AIDS patients had high serum IgA levels (583 vs 250 mg/dl, $p < 0.001$) and lower p15$^+$ ($p < 0.05$) and p55$^+$ ($p < 0.01$) anti-HIV antibodies. The use of these variables for the diagnosis and prognosis of HIV-infected patients is discussed.

THP.117 The Existence of an Inhibitory Factor(s) against HIV-Reverse Transcriptase in Sera from AIDS and ARC Patients.

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We have investigated inhibiting and enhancing effects of HIV infected individuals' sera on HIV-reverse transcriptase (RT) activity in vitro. The modulating effects were not observed in assays containing sera taken from HIV-uninfected homosexuals and heterosexual controls, suggesting that the inhibitory and enhancing phenomena are associated with HIV infection. The presenting study has focused on the inhibitory function of the sera. 4 of 20 (20%) AIDS and 5 of 33 (15%) ARC patients sera showed the inhibitory effect. The effect was not observed in either 20 HIV(-) homosexuals or 28 heterosexual controls. Enzyme kinetic study showed that sera with the inhibitory property lowered the maximum velocity attainable with a given amount of enzyme (Vmax), but did not affect the dissociation constant for the enzyme with its RNA substrates. The result suggests the presence of one or more non-competitive inhibitory factor (s). Furthermore, the inhibitory function of sera was completely absent in the eluates of protein A-agarose affinity chromatography columns. These results indicate that the inhibitory factor is probably an antibody that binds at a site on HIV-RT other than the RNA binding site. In addition, sera from AIDS subjects that displayed RT-inhibiting effects showed significantly greater neutralizing activity than non-inhibitory sera, implying that the inhibitory antibody may contribute partially to the sera's neutralizing activity against HIV infection. The existence of this inhibitor points out several diagnostic problems and therapeutic possibilities.

THP.118 Defective T Cell Mediated Natural Anti-Bacterial Activity in HIV-Infected Patients

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Circulating mononuclear cells (PBM) of healthy subjects possess an in vitro natural activity (NA) against enteropathogenic bacteria, including Salmonella. The effector cell is characterized as a CD4(+)/CD8(-)/Leu8(+) T lymphocyte, acting against bacteria by an ADCC mechanism, via cytophilic IgA. Because AIDS is a profound immunodeficiency caused by human immunosuppressive virus (HIV) involving primarily CD4 lymphocytes, it was of interest to assess NA of HIV-infected subjects at various stage of disease. Results indicate that NA against Salmonella typhi is significantly decreased in AIDS as well as ARC and LAS patients. Worthy of note, CD4(+)/Leu8(+) lymphocytes were previously demonstrated to be the most susceptible subpopulation of T lymphocytes to HIV infection. Anti-S. typhi IgA levels were studied in HIV-infected population and in healthy subjects. Despite an increased level of total IgA, AIDS and ARC patients show a profound depression of specific anti-S. typhi LPS IgA. Therefore, both the cellular and humoral components of anti-Salomonella NA are profoundly depressed. These data can provide an explanation for the increased incidence of bacterial infections in AIDS and ARC patients, including Salmonellosis.

THP.119 Randomized Clinical Trial of Plasma and Recombinant Hepatitis B Virus Vaccines in Gay Men

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A randomized, double-blind comparative study of plasma (20µg/dose) versus recombinant (10µg/dose) hepatitis B virus (HBV) vaccine (both provided by Merck Sharp and Oohme) was conducted in 186 gay men without serologic evidence of prior HBV infection. Vaccine was administered intramuscularly in the deltoid at 0,1, and 6 months; serum was obtained at 0,1,6 and 9 months and assayed for anti-HBs by radioimmunoassay. HIV serologic status was determined by EIA and immunoblot. Results among 158 who received all 3 doses and from whom 9-month serum was available were:

	Plasma		Recombinant	
	HIV neg.	HIV pos.	HIV neg.	HIV pos.
Seroconversion (>20 mIU)	60/69 (.87)	2/8 (.25)	51/72 (.71)	1/9 (.17)
In anti-HBs level				
0	0	0	0	0
1 mo.	0.46	0.09	0.38	0.01
6 mo.	3.09	1.34	2.43	0.67
9 mo.	4.11	1.63	3.48	0.99

Multivariate analysis of data from all 186 participants, with an autoregressive model, demonstrated that the plasma derived HBV vaccine was significantly more immunogenic than the recombinant vaccine, and that HIV infected men were significantly less likely to respond to either vaccine than were HIV seronegative men.

THP.120 Cross-Reacting Neutralizing Antibodies Against Three Different Strains of Human Immunodeficiency Virus (HIV).

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The cross-reactivity of neutralizing antibodies against different strains of HIV is of interest with regard to potential vaccine efficacy. Sera from patients infected with HIV were tested against the III_B, LAV, and RF-II strains of HIV for neutralizing antibodies. The III_B and LAV strains are closely related, but both are distantly related to the RF-II strain. The methods used for this rapid microneutralization assay have been described previously. Briefly, sera and virus were incubated for 90 minutes followed by the addition of Molt-3 cells as the indicator cell line. Four to five days later neutralization was determined by a 50% reduction in giant cell formation. In this system giant cell formation correlates with other parameters of viral replication. To date 15 healthy asymptomatic patients and 8 patients with AIDS have been tested against all 3 strains of HIV. Of these sera, 86% neutralized the III_B strain with a geometric mean titer (GMT) of 1:79 for the positive samples, 78% neutralized the LAV strain with a GMT of 1:75, and 59% neutralized the RF-II strain with a GMT of 1:17. The results obtained with the III_B and LAV strains were 95% concordant. The results obtained with the RF-II strain were 68% concordant with those obtained with the other strains in terms of presence or absence of neutralizing antibodies. The results indicate that HIV often induces cross-reactive antibodies. It is unclear whether a vaccine based on antigens of a single strain would induce immunity protective against distant variants of HIV.

THP.121 Increased B-Cell Activation and Immaturity Associated with Human Immunodeficiency Virus (HIV) Infection

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The expression of phenotypic markers on B lymphocytes in patients with AIDS, in HIV-sero(+) individuals, and in healthy HIV-sero(-) donors was examined by two-color flow cytometry. Patients with AIDS and HIV-sero(+) individuals showed an elevated percentage of B cells (Leu 16+, CD20) bearing an activation marker, the transferrin receptor, when compared to donors not infected with HIV. A decrease in the percentage of resting (Leu 8+) B cells was also seen in AIDS patients and HIV-sero(+) individuals. An increased percentage of circulating, immature (CALLA-positive, CD10) B cells was seen in AIDS patients. These phenotypic changes were accompanied by an increased level of spontaneous IgG and IgM secretion, and increased cell size within the total B cell population, and within some B cell subpopulations, in patients with AIDS and in HIV-sero(+) subjects. These results demonstrate that phenotypic changes indicative of in vivo B cell activation and immaturity accompany the polyclonal production of Ig seen in HIV-infected individuals.

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THP.122 Human Immunodeficiency Virus (HIV) Antigen (Ag) and Antibody (Ab) Profiles in Children with HIV Infection: Correlation with Clinical Status.

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HIV Ag and Ab profiles were determined on sera from 25 children (16♂, 9♀) with HIV infection. 6 children (ages 4-84mos; median 5mos) had CDC-defined AIDS with opportunistic infections (OI); 2 children (ages 12 & 75mos) had histologically confirmed lymphoid interstitial pneumonitis (LIP); 17 children (ages 4-108 mos; median 39mos) had AIDS-related complex (ARC) with persistent generalized lymphadenopathy. HIV p24 Ag was detected in serum by enzyme immunoassay. Western blot analysis of Ab responses to multiple HIV Ags revealed 3 patterns of response: (A) strong total IgG and IgG_1 responses to all viral Ags including p24 and detectable IgA, IgM &/or IgG_{2-4} responses to multiple viral Ags; (B) weak or absent IgG and IgG_1 response to p24 Ag with significant Ab responses to other Ags; (C) weak or absent IgG and IgG_1 response to p24 Ag and at most minimal Ab response to other viral Aga. Clinical status and Ag/Ab profiles are tabulated below.

Clinical Status	p24 Ag			Ab profile pattern		
	++	+	NEG	(A)	(B)	(C)
AIDS with OI	2	3	1	1	-	5
AIDS with LIP	2	-	-	-	1	1
ARC	-	5	11	14	1	1

The presence of Ag in the absence of a significant Ab response to p24 correlates with AIDS and a strong Ab response to p24 Ag plus detectable Ab to other HIV Ags in multiple Ab subclasses correlatea with a more stable clinical status. The longitudinal evaluation of Ag/Ab profiles may help in the assesament of clinical prognosis for children with HIV infection.

THP.123 Frequency and significance of serum monoclonal IgG at various stages of HIV-1 infection.

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A number of HIV-associated abnormalities, such as alteration of regulatory T-cell functions, viral reactivations, B-cell hyperreactivity and B-lymphomas, suggest the possible emergence of B cell derived monoclonality. Indeed, oligoclonal bands have been occasionaly reported in patients with AIDS. A systematic investigation was realized in 150 consecutive patients with HIV-1 infection. Monoclonal immunoglobulins were detected by electrophoresis and immunofixation in agarose. A monoclonal IgG was found in 18 cases (12 %). 20 % of these had at least a second peak. Most of the peaks were IgG K (95 %) and did not exceed 2 g/l. The patients with M-IgG (group I) were compared to the 132 patients without M-IgG (group II), for a 4-15 months observation period. Both groups did not differ in terms of clinical status (asymptomatic carriers, LAS, ARC or full-blown AIDS), above 70 % of the individuals being in both former categories. M-IgG was not related to the presence of Kaposi sarcoma. Blood transmitted HIV (drugs users and transfusions) were slightly more frequent in group I (72 % vs. 42 %). Polyclonal hypergammaglobulinemia was more frequent in group I (71 % vs. 44 %). Mean lymphocyte counts, T4 (760 vs. 618), T8 (930 vs. 757) counts were comparable in both groups. Viral serologies were similarly distributed. During the observation period the M-IgG persisted in 3 patients, disappeared twice. None of the 150 patients had lymphoma. These data confirmed the high frequency of M-IgG, even at early, poorly symptomatic stages of HIV-1 infection, when immune deficiency is likely to be limited. B-cell hyperreactivity was commonly associated without evidence of EBV reactivation. Nevertheless, this study supports the hypothesis that genetic rearrangements of B-cells occur early and frequently, providing favorable conditions for a multistep process of lymphomagenesis.

THP.124 Alpha Interferon of a Marker and a Secondary Pathogenic Factor in AIDS

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Several prospective studies of high risk groups have suggested that alpha interferon (alpha IFN) in an acid labile form, is a marker for the future development of AIDS. In our low dose naltrexone study reported elsewhere at this conference, the mean admission alpha IFN level was 160 i.u. Sixty percent of the patients showed a gradual sequential decline in alpha IFN levels, plateauing at 8 i.u. and 40% showed no such drop. The first group, called responders, had a much higher 12-month survival rate than the nonresponding group, (83% vs 19% $p<.01$) and fewer major O.I.'s ($p<.01$). The results suggest that lowering the pathologically high levels of alpha IFN has a protective effect. Of interest was the finding of an inverse relationship between the admission absolute number of T4's and the admission alpha IFN level in the responder group ($p<.01$) not exhibited in the nonresponder group. These results support the hypothesis that alpha IFN is an important marker both for disease progression and for treatment response. They also suggest that alpha IFN is a major secondary pathogenic factor in the disease. This is supported by the experience with recombinant alpha IFN in animal studies and in clinical trials with cancer patients, demonstrating significant suppression of cellular immunity, including T4 number and function. In addition, alpha IFN acts in vivo as an opioid, and in high levels is likely to down regulate opiate receptors on immunocytes and pituitary beta endorphin production, thereby disturbing endorphinergic correction of immune system dysfunction.

THP.125 Recombinant HIV env Gene Products Induce Human Immune-Specific Lymphocyte Responses In Vitro.

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Peripheral blood mononuclear cell cultures were established from 56 patients with antibody to human immunodeficiency virus. Asymptomatically infected patients (7/11) had significant immune responses induced in culture by an immunoaffinity purified, recombinant glycoprotein (gp-130) from the virus. In addition to stimulating the production of gamma interferon, this recombinant version of gp-120 protein induced transformation responses which predicted clinical disease status as well as correlated directly with circulating levels of helper/inducer lymphocytes (r=0.43, p 0.01) and indirectly with virus antigen (p=0.025). Three of 27 patients with AIDS-related complex (ARC) also responded to this protein. However, these responses occurred significantly less frequently than responses to herpes simplex virus and cytomegalovirus antigens in the same seropositive patients. Neither this protein, nor two other immunoreactive, recombinant HIV proteins induced such in vitro responses in 11 seronegative subjects, thus the antigenic responses are immune-specific. Our findings suggest that HIV-specific cellular immune responses to gp-130 decline in association with disease progression, and become undetectable in frank AIDS. In addition, they appear to serve as a marker for immune responses important in prevention of blood borne dissemination of free virus (as detected by serum HIV antigen assay).

THP.126 Abnormal leukocyte functions in HIV-infected asymptomatic homosexual men with normal CD4+ T-cell numbers

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To investigate early effects of HIV infection on the immune system, we studied leukocyte functions in HIV+ asymptomatic homosexual men (n=14) classified in group II, compared to HIV- homosexual men (n=20). All HIV+ men, except one, had normal absolute CD4+ T-cell numbers, in 7 men CD8+ cells were elevated. CD20+ B cells were low in 5 HIV+ men, monocyte numbers were normal. Compared to HIV- homosexual men, the HIV+ men showed decreased T-cell proliferation induced by CD3 Mab in the presence of normal accessory cells. T-helper activity for polyclonally (PWM)-stimulated normal B cells was decreased in HIV+ but not in HIV- men. Accessory cell function of monocytes in CD3 Mab-induced proliferation of purified normal T cells was decreased in HIV+ men compared to HIV- men. Immunoglobulin (Ig) synthesis in the PWM-driven system by B cells of HIV+ men was severely deficient and was not restored by addition of normal CD4+ T cells or depletion of CD8+ suppressor cells.

In the microculture system (80,000 MNC/well) only MNC of HIV-homosexual men showed spontaneous Ig production. Both HIV- and HIV+ homosexual men showed a decreased abnormal in-vivo antibody response to immunization with Keyhole-limpet hemocyanin. Our results suggest that HIV induces immunological abnormalities before CD4+ T-cell depletion occurs.

THP.127 $T8^+Leu15^-$ Cytotoxic Cells in AIDS-related Diseases in Hemophiliac Patients

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The purpose of this study was to quantitate T cytotoxic cells in HIV seropositive hemophiliac subjects and to correlate these to disease state. Deficient T cell cytotoxicity to viral-infected target cells has been reported in patients with ARC and AIDS. Recently, Nicholson et al reported elevated number of cytotoxic T cells in the blood of HIV-seropositive asymptomatic homosexual men. In our study, the percentage of T8 suppressor/cytotoxic cells were elevated in HIV-seropositive hemophiliacs who were asymptomatic (N=41), had ARC (N=6), or AIDS (N=7) compared to seronegative hemophiliacs (N=24), 44.9, 45.3, 51.8 vs 31.4% ($P<0.01$, <0.01, <0.01, respectively). However, the absolute number T8 cells were not statistically different among these groups of hemophiliacs. Phenotypic analysis of dual-labelled T8Leu15 cells revealed that seronegative hemophiliacs (N=7) compared to normal controls had increased percentage of $T8^+Leu15^-$ cytotoxic cells, 94.2 vs 69% ($P<0.01$). Similarly, seropositive hemophiliacs of all 3 groups had increased percentages of $T8^+Leu15^-$ cells though not statistically different from seronegative hemophiliacs. Seropositive asymptomatic hemophiliacs (N=30), however, had increased number of $T8^+Leu15^-$ cells compared to seronegative hemophiliacs and controls, 704 vs 488 and 301 cells/mm^3 ($P<0.01$, <0.01, respectively). Furthermore, $T8^+Leu15^-$ cells were decreased in hemophiliacs with ARC (N=5), 531 cells/mm^3 (P=NS), and with AIDS (N=4), 259 cells/mm^3 ($P<0.01$). In summary, $T8^+Leu15^-$ cytotoxic cells may be important in controlling HIV infection, evident as an increase in our seropositive asymptomatic hemophiliacs. A decrease of T cytotoxic cells may have predisposed some to develop AIDS or be a reflection of disease activity.

THP.128 DIRECT DETECTION OF HTLV-III ANTIGENS ON LYMPHOCYTES FROM PATIENTS WITH AIDS AND AIDS RELATED COMPLEX.

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Monoclonal antibodies were produced against HTLV-III, the etiologic agent of AIDS and ARC. One of these monoclonal antibodies, designated 3D8, was reactive with the viral core protein (gag), by Western blot analysis against viral lysates and by ELISA assay versus cloned gag product. Antibody 3D8 was used to detect expression of HTLV-III antigens on the H9 cell line following viral infection as well as on lymphocytes from seropositive patients. Virally-infected H9 cells were found to be highly reactive with antibody 3D8 by FACS analysis. Forty-five Western Blot-positive patients representing AIDS, ARC and an asymptomatic group were studied using flow cytometry. A significant percentage of T4-positive lymphocytes from individual patients were stained with antibody 3D8. The highest percentage of HTLV-III positive cells came from patients with AIDS (up to 50% staining of T4 cells) although patients with ARC and patients without symptoms also demonstrated significant expression of HTLV-III antigens. Moreover, there was a correlation between the number of patients expressing HTLV-III antigens on T4 cells and clinical grouping. These data suggest that a higher percentage of T4-lymphocytes express HTLV-III antigens than has been predicted by detection of intracellular HTLV-III mRNA.

THP.129 IMMUNOPHENOTYPES BY FLOW CYTOMETRY: A LONGITUDINAL STUDY IN HEALTHY INDIVIDUALS

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The study was undertaken to assess the variations in the immunological phenotypes of peripheral blood lymphocytes and monocytes in repeated samples from five healthy volunteers who were not at risk for AIDS. Weekly samples were obtained for 13 weeks. Monoclonal antibodies to seventeen lymphocyte and five monocyte antigens were evaluated using two color flow cytometry. Individual and group mean (s.d.) differences were calculated from data for consecutive weeks to determine overall variation. Average week to week differences were less than 5% with the exception of I2+ (17.1%, s.d. 14.7), NKH+ (6.2%, s.d. 4.3), MO1+ (9.8%, s.d. 6.6), and MO2+ cells (7.2%, s.d. 5.4). During the course of the study, one subject had symptoms associated with a common influenza-type viral infection and showed a temporary reversal in the helper/suppressor ratio (0.82) which reverted back to normal (1.83) the following week. Overall, most of the phenotypes remained relatively constant with the exception of those associated with activated lymphocytes, natural killer cells, and monocytes. The observed variations presumably reflected both technical inconsistencies and responses of the immune system to daily environmental stimuli. Because patients also undergo the same types of environmental insults, but may have a more labile immune system, serial phenotypic measurements are essential to adequately assess their immunological status.

THP.130 Oligoclonal IgG bands on Serum-electrophoresis in a Cohort of Homosexual Men in Stockholm, Sweden.

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As part of a health screening project for asymptomatic gay men in Stockholm, sera from 145 men collected 1983 and 1984 were examined with agarose electrophoresis and immunofixation with IgG, IgA, IgM and kappa/lambda antisera (Dakopatts, Denmark). HIV-seropositive men were reexamined in 1985 and 1986. 100 age matched healthy male blood donors served as controls. The results were as follows:

HIV-serology		n	Individuals with oligoclonal bands, (IgG level (g/l))			
1983	1984		1983	1984	1985	1986
NEG	NEG	110	1 (11.2 ± 2.2)	0 (10.9 ± 2.1)	—	—
NEG	POS	10	2 (10.6 ± 1.0)	1 (11.4 ± 1.9)	4 (13.6 ± 2.1)	5 (14.0 ± 1.5)
POS	POS	25	14 (14.8 ± 2.8)	15 (15.4 ± 2.9)	11 (16.0 ± 3.4)	11 (16.3 ± 3.9)
CONTROLS		100	0 (11.6 ± 1.6)			

All the oligoclonal bands consisted of IgG with either kappa or lambda light chains. During the 3 year follow-up 3 of the 25 men, who were HIV-positive in 1983, developed AIDS. All had oligoclonal bands and IgG levels >15.4 g/l in 1983. Oligoclonal bands seem to be a common finding that parallel high IgG levels in HIV-positive gay men. It is not an early finding after seroconversion. Over 50% of the men who were HIV-positive in 1983 had oligoclonal IgG bands and this finding seemed to be constant over the follow-up period.

THP.131 Antibody Response to a Recombinant Hepatitis B Vaccine in Anti-HIV Positive vs. Anti-HIV Negative Persons

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To determine the influence of HIV (Human Immunodeficiency Virus) infection on the outcome of hepatitis B vaccination, 19 homosexuals seronegative (group I) and 8 persons anti-HIV positive (group II) were vaccinated with 20 mcg doses of a yeast-derived hepatitis B vaccine (SmithKline-RIT, Belgium) at months 0, 1, and 6. Another 12 anti-HIV positive persons (group III) with evidence of past exposure to HBV (Hepatitis B Virus) (anti-HBc positive, HBsAg negative; RIA, Abbott) also received a full course of vaccination. Anti-HBs (RIA, Abbott) levels were measured at months 0, 1, 2, 6, and 7.

By month 7, 89 % of group I, but only 3 of 8 anti-HIV positive vaccinees (group II) had seroconverted (p=.005; Chi square test). Increases of anti-HBs levels from month 6 to month 7 averaged 230fold in group I (n=10) but only by factor 8 in groups II (n=2) and III (n=10) (p=.002; Wilcoxon, Mann and Whitney rank sum test).

Total and T4 lymphocyte counts determined at least once during the course of study were significantly higher in anti-HIV negative than in anti-HIV positive vaccinees (mean ± std. dev.; total lymphocytes: 2926 ± 918 vs. 1562 ± 736, p=.002; T4: 1048 ± 413 vs. 398 ± 206, p=.002; respectively).

These data show that this yeast-derived hepatitis B vaccine is immunogenic in population at risk for acquiring HBV and HIV infection, but immune responses as measured by anti-HBs production are impaired in parallel to the decrease of T4 lymphocytes in the course of HIV infection.

THP.132 Lymphocyte circadian cycles in HIV infected individuals : abnormalities of both CD4 and CD8 cells.

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Physiological circadian variations are observed in peripheral blood lymphocytes counts. The nadir occurs around 8.00 a.m. and the peak value at midnight.

In HIV infected individuals, lymphocyte function abnormalities are frequent. So, we developed a protocol to search for modifications in the CD4 and CD8 lymphocyte cycles.

Peripheral blood samples were obtained from 9 healthy controls and 16 HIV infected patients : 9 were asymptomatic or lymphadenopathic seropositive patients (CDC group II-III), 7 were ARC or AIDS patients (CDC group IV).

CD2-OKT11, CD4-OKT4 and CD8-OKT8 cells were determined using fluorescein labelled monoclonal antibodies and a flow cytometer (Spectrum III with a 2140 analyzer, Ortho Diagnostic Systems). Samples were obtained at 8.00 a.m., 4.00 p.m. and midnight. Using absolute number of cells, results were expressed in terms of a "Nycthemeral ratio"(NR) i.e. midnight count : 8.00 a.m. count.

In controls, variations were noted for all lymphocyte subpopulations ; CD4-NR was 1.6±0.4 and CD8-NR 1.4±0.2. In CDC group IV patients, cycles were always impaired : CD4-NR were less than 1.1 and CD8-NR less than 1. In the 9 CDC group II - III patients, 5 had cycles comprised in the normal range, 4 had both CD4-NR and CD8-NR decreased.

It is of interest that there is no correlation between the absolute number of any lymphocyte subset and any NR value. So, CD4 lymphocyte cycle abnormalities were observed even in patients with normal CD4 absolute count. Furthermore, even for CD8 cells (that are not infected by HIV) NR values were low, independently of their absolute count.

Because all CDC group IV patients had lymphocyte cycles abnormalities, the evaluation of NR might become an early prognosis factor. This would be of great interest to CDC II-III group in keeping with their nycthemeral cycles.

THP.133 Zinc Deficiency and Human Immunodeficiency Virus Infection.

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The role of co-factors, including malnutrition, in the observed immunosuppression associated with the human immunodeficiency virus infection (HIV) is unknown. Zinc deficiency predisposes to reversible abnormalities of cell-mediated immunity, as well as thymic atrophy and dysfunction. To assess the possible role of low zinc as a co-factor in the severe immunosuppression characteristic of advanced HIV disease, we measured serum zinc, albumin, and T cell numbers in CDC determined subgroups of HIV infected individuals. Zinc was measured by atomic absorption spectrophotometry. T cell subsets were measured by monoclonal antibodies. Comparisons were for groups versus controls. Results are expressed as mean ± S.D.

	Control	Group II	Group III	Group IVA	Group IVC1	Group IVD
n =	22	7	19	5	14	6
Zinc mcg/dl	1.17±0.2	1.32±0.3	1.05±0.1[c]	0.96±0.1[c]	0.79±0.2[e]	0.92±0.1[d]
T helpers /mm^3	935±376	534±264[c]	675±330[b]	289±317[d]	40±60[d]	104±128[d]
Albumin g/dl	5.12±0.3	4.5±0.5[a]	4.9±0.5[a]	4.3±0.6[a]	3.8±0.8[e]	4.2±0.6[b]
T Test	a=p<0.05	b=p<0.01	c=p<0.005	d=p<0.001	e=p<0.0001	

Group IV patients had significantly decreased zinc levels, which correlated with the decline in immune status, as assessed by T helper cell numbers (r=0.43, p<0.002) Albumin was significantly decreased in all Group IV patients. The etiology of the decrease in zinc with progressive HIV disease is likely multifactorial. We hypothesize that low zinc may exert an additional immunosuppressive effect in HIV disease, and that zinc repletion may have a beneficial role in retarding an otherwise progressive decline in immunity.

THP.134 Human Monocyte Cytotoxicity for Candida Albicans Can Be Augmented with Gamma Interferon and Muramyl Tripeptide.

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Candida albicans (CA) is an opportunistic fungus commonly found in the oral cavity and esophagus of AIDS patients. Monocytes, which may exhibit impaired functional activities in AIDS patients, contribute to host defense against CA. To explore possible mechanisms for augmenting monocyte antifungal activity, we developed a new microassay for measuring cytotoxicity of CA. Monocytes, purified by countercurrent centrifugal elutriation, were cocultured for 4 hr at varying effector to target (E:T) ratios with pulse-labeled (^{3}H-leucine) CA yeast cells (strain 4918). Increasing the E:T ratio correlated directly with increased ^{3}H release and inhibition of CA colony formation. Inhibitors of oxidative metabolism, myeloperoxidase, and phagocytosis caused a marked reduction in monocyte cytotoxicity for CA, confirming in our assay that killing of CA was dependent upon reactive oxygen intermediates and phagocytosis. In experiments designed to determine whether this cytotoxic activity could be augmented, we found that recombinant gamma interferon or muramyl tripeptide (delivered in liposomes) alone did not increase monocyte cytotoxicity for CA but acted synergistically to augment cytotoxicity several-fold.

Thus, the ability to enhance monocyte antifungal activity of CA may have clinical relevance for immunocompromised hosts, in particular AIDS patients with CA and other fungal infections.

THP.135 The Generation of Natural Killer and Lymphokine Activated Killer Cells in HIV-Infected Individuals.

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Individuals infected with HIV usually lack natural killer (NK) cell activity; however, NK activity can be restored in vitro by the addition of interleukin-2 (IL-2). The addition of IL-2 also gives rise to another effector , the lymphokine-activited killer (LAK) cell. We investigated the ability of IL-2 to restore NK as well as to generate LAK activity in 15 patients with AIDS-related symptom complex (ARC) or lymphadenopathy syndrome (LAS) and 8 controls. Freshly isolated peripheral blood lymphocytes (PBL) were assayed for NK against the target, K562, and for LAK against the NK-resistant, Daudi cell line. In addition, PBL were incubated in vitro for 3 days with 50 units of recombinant IL-2 (rIL-2, Cetus Corporation), harvested and assayed for NK and LAK activity.

The results show that freshly isolated PBL from patients lacked NK when compared to control (4.8% vs 25.2%, respectively; $p<0.01$). NK activity was augmented by rIL-2 in all patients and controls; rIL-2 generated LAK in all cases but one patient. There was a high degree of correlation ($r=0.91$) between the increment in NK by rIL-2 and the generation of LAK. These data suggest that the same cell may mediate NK and LAK following incubation with rIL-2. Studies are in progress to explore the generation of NK and LAK by HIV antigens as well as to investigate their effectiveness in the lysis of HIV-infected targets.

THP.136 A study of some immunological parameters in relation to HIV antigenemia in patients infected by HIV

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The relation between infection with HIV and various immunological parameters was studied in the following groups of individuals: a) healthy controls; b) homosexual individuals from the AIDS risk group without anti-HIV antibodies; c) idem, but with anti-HIV antibodies; d) patients with lymphadenopathy syndrome; e) patients with ARC; f) patients with AIDS and opportunistic infections. Each group, consisting of 15-20 individuals was tested for: absolute numbers of T4- and T8-positive cells; ratio T4/T8; and cellular immunity both in vivo and in vitro. Healthy HIV-antibody positive individuals and patients with LAS showed aready a decreased ratio T4/T8, mainly due to an increase in the number of T8-positive cells. The ratio in ARC and LAS was even lower but now due to low numbers of T4+ cells and with normal numbers of T8+ cells. The lymphocyte proliferative response, low in the HIV-antibody positive group, was normal in the LAS group but profoundly decreased in the ARC and AIDS group. In the HIV-antibody positive group the severity of the impairment of the various parameters of immunocompetence was not related to the presence of antigenemia. Compared to healthy controls the antibody response after immunization with KLH was depressed (although not absent) in all groups studied.

THP.137 Prevalence of HIV among the Infectable Drug Using Population in South London and Factors Influencing its Spread.

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This study surveys the HIV antibody status of 250 infectable drug abusers in South London and includes a more detailed analysis of 100 of those tested. It evolved from a clinically perceived need to identify rapidly common risk factors when HIV antibody testing to include in local health education campaigns. The subjects are a mixed sample comprising those who are or were involved with various agencies and those still on the street.

The overall study also looks at the general drug taking behaviour of the subjects, with particular reference to their injecting and sharing habits, together with other facts which could influence or facilitate the transmission of the virus within the population.

The more detailed survey focuses on past and continuing drug abuse and its associated behaviour, together with an analysis of changing sexual behaviour and behavioural modification linked to the awareness of the virus and its differing modes of transmission. This gives insight in the way the virus has passed from particular at risk communities to the more general non-drug abusing population.

The surveys are being conducted over an 18 month period. They demonstrate a five-fold increase of HIV infection in this previously HIV-free population, over the first 12 months of the study alone. Revised figures will be included in the survey in time for the Conference.

THP.138 Financial Analysis of AIDS Programs in the Americas

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PAHO and WHO expect to receive approximately $200 million in fiscal year 198B for AIDS control in developing countries. To be able to make and evaluate financial commitments of such funds there is need to develop a financial system with national program and activities components. The national system compiles the level and uses of funds by year for all activities in the country, while activities monitoring systems compile these data for individual program activities, and relates funding to outputs. For the national system a matrix reporting system is proposed for each year with sources (international and domestic agencies) and uses of funds (types of AIDS program activities such as case finding, contact tracing, screening, treatment, education, and research). The activities monitoring system relates expenditures to the country's reporting system on the magnitude and trend of the AIDS problem in the country (cases diagnosed and number of deaths) and to specific indicators (e.g. number of repeatedly positive serological tests).

A preliminary application to San Juan, Puerto Rico and Sao Paolo, Brazil, suggests that AIDS case management and treatment is being financed primarily from general operating expenses of public hospitals, with the likelihood of reducing funds for all other treatments.

This framework is proposed as a tool for donors and national and state governments to monitor uses of funds, target requests to needed areas, and constantly improve the productivity of their expenditures.

THP.139 HIV Infected African Patients With a Negative HIV ELISA Serology?

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In both healthy carriers and AIDS patients commercially available ELISA kits will not detect all Western blot(+) persons. Sera of all HIV(-) (Organon Teknika) patients with persistent diarrhea (n=25), a history of herpes zoster (n=15), a generalized pruritic papular eruption (n=9) or a generalized aggressive Kaposi's sarcoma (n=1), observed at Mama Yemo Hospital, Kinshasa, between June 1985 to October 1986, were tested by Western blot. The sera of 10 (20%) of the 50 HIV ELISA(-) patients with AIDS-like symptoms or signs had at least the protein band p 24 on Western blot (Du Pont strips). In 2 (4%) of these 50 patients, Western blots showed the presence of at least the p 24 and the gp 41 band. In one ELISA and Western blot(-) patient with persistent diarrhea, esophageal candidiasis was found endoscopically. In the 3 HIV ELISA(-) patients in whom cultures were performed, HIV was isolated. The sera of two of these patients were Western blot(-) and in the other, only a p 24 protein band was present. Antibody tests using other ELISA methods, LAV II and HTLV IV serologies are pending.

Performance of Western blot tests should be considered when evaluating suspected HIV(-) cases of AIDS. Furthermore patients may be HIV virus carriers without the presence of HIV antibodies detectable by either ELISA or Western blot.

THP.140 The Effect of Pregnancy on Progression of HIV Related Disease.

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It has been suggested that pregnancy adversely affects the outcome of HIV infection due to the physiologic immunosuppression that occurs late in pregnancy. We are prospectively studying the effect of pregnancy on the natural history of HIV infection in intravenous drug abusers attending a NYC methadone program. Women of child bearing age without AIDS or oral thrush(OT) are serially tested for HIV antibody(Ab), T-cell analyses and viral culture. Physical examinations and standardized interviews are performed. Pregnancy is identified early by routine monthly urine testing. Seropositive(SP) women delivering livebirths or carrying >24 weeks are compared to women who did not become pregnant or who terminated pregnancy by 13 weeks gestation.

Of 276 women tested since July 1985, 96(38%) were SP. Of these, 34 have been rescreened over a mean 12 mos. of follow-up. Among the rescreened, 15 (Group I) had pregnancies carried >24 weeks and were followed a mean of 6 mos. post-partum and 19 (Group II) either did not become pregnant (14) or had pregnancies terminated by 13 weeks gestation (5). The two groups were stratified by the absence or presence of generalized lymphadenopathy (GL) initially and followed for progression to GL, OT, or AIDS.

Group	Baseline Status	No. Subjects	No. Progressed	Mean Mos. F/U
I	without GL	12	6/12 GL only*	11
	with GL	3	1/3 OT**	10
II	without GL	7	2/7 GL only*	15
	with GL	12	2/12 OT**	12

*p>.05 **p >.05

No subject developed AIDS, although 7/15(47%) in Group I vs. 4/19(21%) in Group II advanced in their HIV status (OR=3.3, p<.07). These preliminary data suggest that pregnancy was not associated with the occurrence of AIDS. Further study may confirm the trend of greater HIV disease progression due to pregnancy.

THP.141 Pancreatic Disturbances and AIDS : an Anatomopathological Study
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A systematic analysis from autopsy of 113 AIDS patients has enabled us to confirm the existence of alterations of the pancreatic gland in about half of them. The cases studied were 99 men and 14 women whose average age was 36.8 years (22-71). Among them were 82 homosexuals, 25 Africans or Haitians, 3 drug abusers, 1 transfused patient, 2 without risk factors. An average of 12.4 months elapsed between the discovery of the disease and death. Sixty seven patients had had isolated opportunistic infections, 7 a isolated Kaposi sarcoma of lymphoma, and 39 had had both. Macroscopically the pancreas was normal in 59 cases ; 54 patients showed alterations of the gland such as oedema and increase of volume (40), fibrous aspect (5), cytosteatonecrosis lesions (8), kaposian of lymphomatosis aspect (5). Histopathology revealed that in 16 cases the pancreas could not be interpreted because of necrosis, alterations were found in 49 cases, aspects was normal in the remaining 49 cases. The main alterations were largely disseminated. The forms were cytosteatonecrosis (8) or subacute pancreatic disorder with inflammatory lesions (oedema, polymorphic granuloma) (33), fibrosis (14), metaplasia and dedifferentiation of the ducts (14) or vascular lesions (haemorrhage, thrombosis) (8). Specific lesions were observed in 21 cases, though non could be found in 28 cases. Such lesions, disseminated both in the exocrine and endocrine tissues and in the interstitial and ductical ones, were as follows : cytomegalic inclusion cells testifying to CMV infection (10), cryptococcal (2), tuberculous lesions (1), kaposian sarcoma or lymphoma (8). In 19 cases specific lesions demonstrated were correlated to the clinical findings.

The pathological processes observed histologically can be regarded as partially responsible for the disorders of the digestive system characteristic of AIDS.

THP.142 The Humoral Immune Response in HIV-Associated Periodontitis.
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We have recently observed an acute, painful and rapidly progressive periodontitis in HIV-infected individuals, which we have termed AIDS-virus associated periodontitis (AVAP). Little is known about the etiology and pathogenesis of this infection. The purpose of this investigation was to provide insight into the oral microbioata associated with the lesion. Since direct culturing of the associated flora is time consuming, expensive, and complicated, we chose to evaluate the systemic immune response to potential pathogens of AVAP. For this prupose we studied the immune response to the following potential periodontal pathogens: Bacteroides gingivalis (33277), Fusobacterium nucleatum (10953), and Capnocytophaga sputigena (33123). An indirect ELISA assay was used to measure the level of antibody (Ab) in HIV-seropositive homosexuals, HIV-seronegative homosexuals and HIV-seronegative heterosexuals. Formalinized, whole bacteria were used as antigen in wells of polystyrene microtiter plates. After blocking unbound antigen sites, serial dilutions of serum were incubated, washed and blocked. The secondary Ab was Mouse Anti-Human IgG [Fc] Fragment, and the tertiary Ab was alkaline phosphatase conjugated Goat Anti-Mouse IgG F(ab')2. Substrate was added and measurements taken at OD405. A reciprocal dilution of serum required to provide a reading of 0.4 at OD405 was calculated for each patient. Means with standard deviations were then calculated for each group tested, and a t-test was applied to determine significance. Results for B. gingivalis indicated a significantly higher antibody titer for HIV-positive homosexuals than for HIV-negative homosexuals ($p<.05$), and heterosexuals ($p<.001$). For the same groups of people, results for F. nucleatum indicated a higher titer, $p<0.005$ and $p<.01$ respectively. Interestingly, the results indicated no significant difference between the same groups of individuals for C. sputigena. Results demonstrate that bacteria normally associated with periodontitis in normal individuals are causing elevated systemic antibody levels in HIV seropositive individuals. Thus, these bacteria may be overwhelming the immunocompromised patient to cause AVAP. Supported by NIH Grant T35DE07103.

THP.143 Cresyl Violet: A Rapid and Sensitive Stain for Diagnosing *Pneumocystis carinii* Pneumonia by Sputum Examination.
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The detection of *P. carinii* cysts in the sputum of patients with the Acquired Immunodeficiency Syndrome (AIDS) has been useful in diagnosing *P. carinii* pneumonia noninvasively. Gomori Methenamine Silver (GMS) has the advantage of staining the characteristic cyst (which is the most commonly recognized form). However, it is time consuming, technically involved and may be relatively insensitive for detecting small numbers of cysts in sputum.

One hundred and ten expectorated sputum samples were collected consecutively from 90 patients with AIDS and unexplained pulmonary infiltrates. Each specimen was cytocentrifuged onto two slides. One slide was stained with GMS and the other with Cresyl Violet (CV). All slides were read by two independent observers in a double blind fashion.

Of 110 specimens, 27 (25%) were positive for *P. carinii* cysts by CV, and 17 (16%) were positive by GMS. In 6 of the 10 patients whose sputa were positive by CV, but negative by GMS, *P. carinii* was confirmed (by histology in 5 patients and by a typical clinical picture with response to specific therapy in 1 patient). In 4 of the 10 patients, 3 had no follow-up and one had no clinical evidence of *P. carinii* pneumonia.

These results suggest that CV is more sensitive and as specific as GMS in detecting *P. carinii* cysts in sputum. CV staining of sputum is technically simple and takes only 30 min. to perform, while GMS is technically more difficult and takes 3 hrs. to perform. Since CV stains the easily recognized *P. carinii* cyst form (and not the much smaller trophozoite), it requires less special expertise than other rapid staining techniques for *P. carinii* (i.e. Giemsa stain). CV may be a superior stain for diagnosing *P. carinii* pneumonia by sputum examination. In patients with AIDS it could be easily adapted for general use to expedite diagnosis and treatment.

THP.144 Combination chemotherapy (low dose adriamycin,bleomycin,vincristine) for advanced Epidemic Kaposi's Sarcoma (EKS).
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Thirty homosexual men with advanced EKS were treated with combination chemotherapy consisting of adriamycin, 10 mg/m2 (n=14), or 20 mg/m2 (n=16), plus vincristine, 1.4 mg/m2 and bleomycin, 10 mg/m2,given IV every two weeks. At study entry, extensive cutaneous EKS involvement was present in 29, in whom 19 had associated lymphoedema; mucous membrane involvement was present in 17, symptomatic gastrointestinal disease in 5, lung involvement in 12. Systemic "B" symptoms were present in 17, and hx of past pneumocystis carinii pneumonia in 5. At study entry, mean hemoglobin (Hb) was 12.7 gm/dl(r=9-22); mean absolute neutrophil count was 2886/dl (r=1073-6724); mean lymphocytes were 1329 (r=377-3190), mean T4=146dl (r=10-412); mean T4:T8 =0.2 (r=0.03-0.8). Chemotherapy was begun at a median of 4 mos from initial dx (range=0-10 mos). Response rate was 78.6%,with complete response in 14%, partial response in 64%. An additional 18% had minimal response, while one patient had no response, and two are too early to evaluate. Poor prognostic indicators for survival include current or past hx of diarrhea ($p=.03$) and "B" symptoms ($p=.02$). Involvement of any particular visceral organ had no impact on response rates or survival. Toxicity included nadir mean Hb of 11.4 gm/dl, neutrophils of 1589/dl (324-5530), opportunistic infections in 7 pts. Median survival was 8 mos. Because of these early results in pts with extremely advanced disease, we have begun a prospective, randomized trial of adriamycin alone (20 mg/m2) vs. ABV. Results will be presented. We conclude: (1) Low dose adriamycin, plus vincristine and bleomycin may induce remissions in 79% of pts with advanced EKS. (2) In spite of good responses, survival may be short, often due to other complications of AIDS.

THP.145 Bacterial Infections In Human Immunodeficiency Virus (HIV) Infected Children.
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HIV infection in children is frequently complicated by bacterial infection, and preventive immunoglobulin (IG) therapy has been suggested. In a 3.5 year period we have cared for 70 HIV infected children (only 3 of which were treated with IG); 44 of whom had at least one bacterial culture. There were 1163 cultures performed in these 44 patients: mean = 26.5, median = 15, range 1-126 cultures per patient. There were 97 documented episodes of bacterial infection in 26/44 (59%) of these patients (mean = 3.7, median = 2, range 1-11). Otitis media, pneumonia, urinary tract infections and diarrhea were the predominant syndromes identified. There were 31 bacteremias among 17 patients (mean = 1.8, median = 2, range 1-5). Pneumococci were the most common blood isolates (11/31), and types 4,6,9,14 and 19 were recovered. One patient had 3 separate episodes due to the type 6 organism. Other organisms included: P. aeruginosa 2, E. cloacae 2, K. pneumoniae 2, S. aureus 2, S. viridans 2, enterococcus 2; and one each of Streptococcus group A and B, S. epidermidis, P. maltophilia, E. coli, A. calcoaceticus, S. enteridiidis, bacillus species, and diptheroids. One patient had concurrent E. cloacae and enterococcal bacteremia.

Overall 26/70 (37%) of patients with recognized HIV infection have had bacterial infection and 17/70 (24%) have had bacteremia, all of which were associated with infection at other body sites. One of our 3 IG treated patients developed Klebsiella sepsis. Bacterial infection could be implicated in the deaths of only 4 patients: 1 with enterococcal and varicella pneumonia, 1 with E. cloacae, fungal and CMV pneumonia, 1 with Pseudomonas and PCP, and 1 with pneumonia due to Pseudomonas only. Although bacterial infections are a frequent cause of morbidity in HIV infected children, they are usually treatable. IG therapy might have been expected to prevent the pneumococcal infections, its' role in preventing other bacterial infections is less clear.

THP.146 Neuropsychological Characterization of HIV Infection.
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Reports that the brain may be directly and selectively affected by HIV infection has increased the importance of neuropsychological characterization of AIDS dementia in patients without opportunistic infections of the brain. We previously observed significant differences in the performance of a group of 13 patients with AIDS but without CNS opportunistic infection compared with 10 age and education matched homosexual volunteers on neuropsychological tests sensitive to alterations in attention and motivation. In addition differences were found on tests measuring functions that are normally considered most resistant to global brain insult such as the vocabulary subtest of the verbal IQ. While no significant differences between the groups were found on tests assessing memory, both groups performed poorly on tests of verbal memory, scoring significantly below established norms. Similar findings have been observed in an additional 12 AIDS patients compared with 8 seropositive-only patients and 8 patients with chronic active hepatitis. These results suggest a two factorial component to the neuropsychological profile of AIDS patients, one component associated with attention and motivation, another with knowledge functions. The results additionally suggest that brain areas subserving language related functions may be selectively affected by the HIV infection, with the degree of impairment perhaps reflecting the status of the infection. Comparison of AIDS patients with Huntington's and Alzheimer's patients will be made to evaluate similarities and differences in their dementias.

THP.147 Assessment of Potential Chemotherapeutic Agents Against Mycobacterium avium Complex Infections in Beige Mice

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Mycobacterium avium complex (MAC) organisms are major opportunistic pathogens afflicting AIDS patients. Using the beige mouse model, we have investigated the chemotherapeutic potential of 20 compounds which showed high in vitro antimycobacterial activity against numerous strains of MAC. The in vivo chemotherapeutic activity of each of these compounds was assessed in beige mice challenged intravenously with a virulent MAC strain, in each of 2 or 3 experiments. Comparison of the mortality and CFU counts of organisms from spleens and lungs at various periods of challenge between the drug-treated and control groups, enabled us to classify these 20 compounds into three groups: active, probably active and inactive. Activity in vivo was defined as a statistically significant reduction in the mortality and CFU counts of the organisms recovered in the drug treated group as compared with the controls; inactivity was defined as having no evidence of any difference at any point between these two groups. Drugs in the probably active group indicated some activity after prolonged chemotherapy, suggesting that perhaps with higher doses, these drugs would show more significant activity. By this classification, 4 drugs, amikacin, CQQ (gangamicin), clofazimine and rifabutin were classified as active; desoxyfructoserotonin and cyclopentyl rifampin as probably active; and the remaining 14 as inactive. These studies were extended to combination chemotherapy among these 4 active drugs. (Supported by NIH Contract No. 42544).

THP.148 Preliminary observations of the effect of cow's milk globulin upon intestinal cryptosporidiosis in AIDS.

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Many of the intestinal (GI) complications of AIDS result from immune deficiency in the gut. Impaired secretory immunity in AIDS (Dig Dis Sci 32:129,1987) could affect the clearance of parasites from the GI tract. In this report, the preliminary observations of the effect of cow's milk immune globulin (Stolle Research and Development Co) upon the course of chronic intestinal cryptosporidiosis in AIDS is presented. The globulin was prepared from the milk of cows that had been hyperimmunized with human enteric bacterial antigens (but not cryptosporidium) using a proprietary, slow release vaccine. The milk was pasteurized at low temperature under reduced pressure to prevent protein denaturation, then was passed through a membrane to retard molecules greater than 100,000 MW and concentrated 30 fold. Three patients were treated. All had diarrhea with cryptosporidia in stool samples and on intestinal biopsy. Patients were treated with ascending doses of the globulin given orally qid, with $NaHCO_3$. All 3 responded favorably, with the reappearance of some or all formed stools. Stool examinations reverted to negative in 2 patients tested and organisms disappeared from intestinal biopsies in 1 of 2 tested. While preliminary, the results strongly suggest that a large molecular weight fraction in cow's milk effectively suppresses cryptosporidiosis in patients with AIDS.

THP.149 NORFLOXACIN IN THE ERADICATION OF SALMONELLA INFECTIONS IN AIDS PATIENTS.

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Recurrent episodes of salmonellosis, including recurrent life-threatening bacteremias, have been well-described in patients with AIDS. Because of the need to avoid sensitization to trimethoprim/sulfamethoxazole (TMP/SFX) in AIDS patients and the high frequency of ampicillin resistance of salmonella isolates, alternative therapies must be sought. We report the treatment of three AIDS patients, who had recurrent salmonellosis, with norfloxacin, a new oral fluoroquinolone which has excellent in vivo activity against Salmonella sp. Each patient had 2-3 prior distinct clincal episodes of salmonellosis which had failed to be eradicated with standard courses of ampicillin, TMP/SFX, ceftriaxone, or cefotaxime. Microbiologic relapse occurred in each patient within 2-4 weeks. Each of the salmonella strains was susceptible to norfloxacin. Patients were treated with norfloxacin 400 mg bid orally for 30 days. Stool cultures were negative at one week in all three patients. No adverse reactions to norfloxacin were noted during the treatment period. Patients #1 and #2 remained culture negative during a 4-6 week followup period and had no clinical recurrences until their deaths from other AIDS-related infections or neoplasms. Patient #3 had a clinical and microbiologic relapse of salmonella 1 week after norfloxacin was stopped but responded clinically to retreatment with norfloxacin. Norfloxacin appears effective in the treatment of salmonella infections in AIDS patients and may be more useful than standard agents in eradicating the organism and preventing clinical and microbiologic relapse. Oral administration and twice daily dosing are significant advantages. Further studies will clarify its role in the management of salmonellosis in AIDS patients.

THP.150 Disseminated Histoplasmosis in Patients with AIDS or at high risk for AIDS.

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Four patients with AIDS and 1 at high risk for AIDS living in Los Angeles, CA. developed disseminated histoplamosis. None of the 5 patients had recently been in a highly endemic area for H. capsulatum and only 2 patients had ever been in such an area in the distant past. Histoplasmosis was the initial AIDS defining condition in 4 patients. All patients had constitutional symptoms of weight loss, fatigue, night sweats and unusually high fevers. Chest radiographs and liver functions tests were abnormal in all patients. Cultures of bone marrow in 2 of the 3 patients tested, blood cultures in 2 patients, and biopsies of brain, adrenal gland, and lymph node yielded H. capsulatum in separate patients. Four patients died; only 1 patient lived more than six months despite antifungal therapy with amphotericin B.

A review of the literature showed 54 patients with AIDS and histoplasmosis from all areas. Disseminated histoplasmosis was the initial AIDS defining condition in 31 of 43 patients in whom such data were given. Commonly involved sites were blood, bone marrow, liver, spleen, lymph nodes and lungs. Serological tests were of little value. Improvement during therapy with amphotericin B occured but outcome was very poor; relapses during ketoconazole therapy were common.

Disseminated histoplasmosis is an important cause of morbidity and mortality in patients with AIDS or at risk for AIDS, including those in non-endemic areas.

THP.151 Multiple-Dose Pharmacokinetics of Eflornithine in AIDS Patients Treated for Pneumocystis carinii Pneumonia.

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Eflornithine (alpha-difluoromethylornithine, DFMO) is an irreversible inhibitor of ornithine decarboxylase. We have previously reported eflornithine's efficacy in treating refractory Pneumocystis carinii pneumonia and the occurrence of severe thrombocytopenia in patients with impaired renal function. Others have reported that the elimination of eflornithine is highly dependent on renal function and so information about multiple-dose eflornithine pharmacokinetics in patients with AIDS is needed to modify dosage and avoid toxicity.

The biodisposition of eflornithine was studied in detail in four AIDS patients receiving compassionate therapy for refractory Pneumocystis carinii pneumonia. Intravenous treatment with 100mg/kg IVPB every 6 h was given for 3 to 5 days. Serum for eflornithine assay was then obtained before and 0.5, 1.5, 3, 6, and 12 hours after a dose, while the subsequent dose was withheld. A high-pressure liquid chromatographic assay was used to measure eflornithine concentrations. Pharmacokinetic parameters were determined using a one-compartment model.

Creatinine clearance ranged from 75.7 to 101.2 ml/min. At steady-state, peaks ranged from 196.6 to 317.9 mg/L and troughs ranged from 71.3 to 113.3 mg/L. Pharmacokinetic parameters (mean $\pm$ SD) were: distribution volume (Vd) 32.8 $\pm$ 4.4L, half-life (t1/2) 4.1 $\pm$ 0.5 hours, elimination-rate constant (Kel) 0.17 $\pm$ 0.02, and total body clearance (CLtb) 92.3 $\pm$ 9.9 ml/min. A one-compartment model is appropriate to evaluate the relationship between eflornithine pharmacokinetics and renal function in AIDS patients.

THP.152 Histologic Patterns of Lymphadenopathies in AIDS: Correlations with Progress of Disease.

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Persistent generalized lymphadenopathy (PGL) is one of the manifestations of infection with immune deficiency virus (HIV) which often precedes the severe opportunistic infections and neoplasias of acquired immune deficiency syndrome (AIDS). We examined microscopically biopsied lymph nodes of 60 patients, identified characteristic histologic lesions and correlated them with the presence of HIV antibodies, T_4/T_8 lymphocytes ratios and the progress of disease. There were 55 men and 5 women, with a mean age of 37 years. A follow up of 3 months to 8 years showed that 37 patients progressed to AIDS including 23 who died while 23 remained in the stage of PGL. The lymph nodes were classified in 3 types according to predominant histologic patterns:
A. hyperplasia of lymphoid follicles with germinal centers showing cytolysis and phagocytosis. B. effaced follicles, diffuse lymphoid and vascular hyperplasia. C. atrophic fibrosed follicles, lymphoid depletion and hypervascularity. The predominant lymph node pattern in 1981-83 was type A while in 1984-86 type C was more frequent. More patients with types A and B remained stationary PGL whereas more type C patients died of AIDS. Patients with type B and C lesions more often developed Pneumocystis pneumonia, CMV infections and lymphoma. Nine patients had repeated biopsies which in 3 cases showed persistance of types A and B for up to 2 years and in 6 cases progression from types A and B to C. Lymph node lesions type C consistently correlated with short survival, types A and B with better prognosis.

THP.153 Scales for the Neurological Examination and History in the AIDS Dementia Complex

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The AIDS dementia complex (ADC) is a frequent complication of HIV infection which usually develops after the systemic manifestations of HIV infection, but at times will precede AIDS and apparently pursue an independent course. In order to more clearly define the epidemiology, natural history and response to therapy of the ADC, we have attempted to develop standardized neurological history and examination scales to complement formal neuropsychological testing. These involve ADC-directed questions related to cognitive, motor and behavioral dysfunction that are oriented toward functional status. The neurological examination is also scaled to evaluate these same functions by mental status, motor and coordination tests. A long form of this examination has been developed for detailed assessment of neurological natural history and the response to antiviral therapy, while a short form has been developed for larger-population epidemiological studies and for screening examinations. We have begun to use these scales together with standardized functional status scales and neuropsychological tests in HIV-infected individuals ranging from clinically asymptomatic to severe ADC. Preliminary analyses suggest that these neurological history and examination scales correlate with traditional functional status scales (e.g., Karnofsky, Kurtzke and Blessed) as well as with formal neuropsychological evaluation (correlations ranging from r = .4 to r = .75). These instruments, which will be described in detail, have the advantage of being brief, ADC-specific scales.

THP.154 Prognosis and Natural History of Pneumocystis Carinii Pneumonia: Indicators for Early and Late Survival

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Prognostic indicators of 74 consecutive patients (pts) with first episode of Pneumocystis carinii pneumonia (PCP) at San Francisco General Hospital (SFGH) from March through August 1985 was reviewed, a time before AZT therapy became available. All pts were in a high AIDS risk group, had no evidence of non-AIDS immunosuppression, and were men with a mean age of 36 years (range 22-59). 23% of the group already had an AIDS diagnosis, usually Kaposi's sarcoma, at presentation with PCP.

Kaplan-Meier survival analysis showed that 27% (+5%) died within the first four weeks after first PCP episode. Pts with initial room air arterial blood gas PO2 < 60 torr had 4 week mortality of 50% versus 14% with PO2 > 60 (p=.03). Type of initial drug therapy (trimethoprim / sulfa-methoxazole 68%, Dapsone 20%, Pentamidine 9%, other 3%) was not predictive of early or late mortality. Median survival after first episode was 9.8 months. Probability of a second episode of PCP was estimated at 18% at 6 months, 46% at 9 months, and 65% at 18 months. The second episode mortality at four weeks was 37% (+10%): overall median survival was 4.8 months.

To create a group comparable to populations eligible for clinical trials after PCP, survival and progression was recalculated for pts living at least 4 weeks after initial episode. 6 month mortality was 18% (+6%) and 6 month recurrence was 18% (+6%). When planning sample sizes for trials of post PCP pts, the correct clinical subset must be used to estimate expected survival.

THP.155 AIDS Dementia Complex associated with Brain Reactive Antibodies

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The cause(s) of AIDS dementia complex are unknown. It has been suggested that dementia may be a result of direct neurologic infection by HIV,or an indirect effect, such as autoimmune phenomenon. Although HIV has been detected in the CNS, the target cell/s appear to be macrophages and/or glial cells but not neuronal tissue. Brain reactive antibodies (BRAs) are present in patients with dementing diseases such as Alzheimer's disease and Cruetzfeldt Jakob disease. We present evidence that BRAs are associated with AIDS dementia. Electroblots prepared from normal human hippocampal tissue were used to analyze BRA activity. Thirty sera samples from HIV seropositive patients,18 with and 12 without AIDS dementia complex were screened for BRAs. The results reveal that 78% of patients (14/18) with dementia, and 33% of patients (4/12) without dementia were positive for BRAs (X^2=4.22, p<.04).The brain reactive protein in hippocampal tissue has an apparent M.Wt of 45 kDa. We had observed earlier that although 16-30% of normal subjects also have BRAs,the activity is rarely directed against the 45kDa protein.The presence of antibodies in patients without AIDS dementia complex suggests that BRAs may be an early marker of dementia.However, prospective studies need to be performed to evaluate the role of BRAs in AIDS dementia complex.

THP.156 Outcome of Subsequent Pregnancies in an HIV Seropositive Woman.

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We have previously documented that human immunodeficiency virus (HIV) infected women with one infected child have a 66% of transmitting the virus in subsequent pregnancies. It has also been postulated that the physiologic immunodeficiency of pregnancy may exacerbate the disease process. We report a 32 year old intravenous drug abusing woman seropositive for HIV who has a 5 year old son with AIDS. This woman has been clinically well though she was immunodeficient as documented by reversed T4/T8 ratios and abnormal in vitro lymphocyte mitogenic transformations. Two subsequent pregnancies have produced two HIV uninfected children. Her immune aberrations have disappeared and her immune studies remain normal even though she is 20 weeks pregnant. This patient may represent a self reversal of clinical and immunological pathology.

THP.157 Immunotoxicological Properties of Isobutyl Nitrite

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Acquired Immunodeficiency Syndrome (AIDS) is frequent among homosexual men who use licit and illicit drugs recreationally. We have investigated the immunotoxicological properties of one such illicit drug, isobutyl nitrite (IBN), in street gargon "RUSH" in beige and C57Bl/6 mice. Beige mice in general tolerated a less period of exposure to IBN as compared to the C57Bl/6 mice. Beige mice were infected intravenously Mycobacterium avium complex (MAC) and exposed daily, alternate day and twice weekly. The groups having daily inhalation showed high and early mortality (90%) and high CFU counts in the spleen and lungs with progressive decrease in alternate day and twice weekly groups. Oral and rectal routes of challenge with MAC showed similar trends. Mortality with and without IBN exposure were 90 and 40, 30 and 0 and 30 and 0, between IBN treated and controls respectively, with IV, oral and rectal challenges. Statistically significant differences in CFU counts of MAC were seen between IBN treated and control animals in all series. Exposure to 0 to 1% of IBN showed a dose related toxicity on viability of macrophages and lymphocytes from beige and C57Bl/6 mice. At the optimal concentration, it caused diminished phagocytic indices and greater intracellular growth of the organisms in peritoneal and alveolar macrophages. Exposure of beige and C57Bl/6 mice for 2 to 4 weeks caused increased release of superoxide anion (O_2^-) and hydrogen peroxide (H_2O_2), decreased NK cell activity but no change in the TH:TS cell ratios. Toxicity of IBN may operate either through diminution of NK cell activity or through increased release of H_2O_2, which in turn, can form toxic complexes with methemoglobin which is a consequence of IBN administration. (Supported by Research Grant NO. AI-21897 from NIH).

THP.158 Prospective Neurodevelopmental Outcome of Infants of HIV Seropositive Mothers and Their Controls.

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As part of a prospective neurodevelopmental follow-up, the development of 18 HIV persistantly seropositive infants is compared to that of 28 seronegative controls. The sample is drawn from 2 patient populations: infants whose mothers attend a special substance abuse pregnancy clinic (13 pos; 18 neg) or a Haitian pregnancy clinic (5 pos; 10 neg). Thirty-five infants have been assessed at 1 month of age using the Einstein Scale; 23 at 3 months and 13 at 6 months using the Bayley Scales, by an examiner blind to the infants' status. Correcting for gestational age, 6 seropositive infants and no controls were found to be developmentally delayed (p<.05).

No differences were found between the groups at 1 month of age. At 3 months, mental development scores were lower in the positive group (x=101) than the controls (x=109; p<.05).

The 6 month sample is comprised of infants of substance abusing women only. The seropositive infants had poorer language development (p<.025) and a trend for poorer cognitive development (p<.075) than the controls.

Two additional infants, born to seropositive mothers, seroreverted before 6 months of age. Their data is not included in the above analysis; their development is within normal limits.

Infants exposed to HIV appear to show specific delays and/or lowered developmental quotients by 3 months of age.

THP.159 Does Concomitant HIV Infection and Measles Infection in African Children Lead to Increased Morbidity and Mortality?

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To determine if concomitant measles and HIV infection augment childhood morbidity and mortality, we are studying 300 children less than 6 years old admitted with clinical measles to Mama Yemo Hospital in Kinshasa, Zaire between Jan-April, 1987. Measles cases are confirmed by IgM serology while HIV infection is established by detection of HIV antibodies by repeat ELISA with Western blot confirmation. From Jan. 8-29, 62 children have been enrolled (34 males, mean age = 15.5 months; 28 females, mean age = 18.6 months) of whom 5 are HIV seropositive (8%). Of the 5 HIV seropositive children, 2 (40%) have died, and 3 (60%) have improved during hospitalization. Among the 57 HIV seronegative measles cases, 7 (12%) have died and 50 have improved. History of measles vaccination was low among both groups with 1 HIV positive (20%) and 8 HIV negative (14%) children having previously received measles vaccine. HIV seropositive children were more likely than HIV seronegative children to present with polyadenopathy (60% vs. 42%), a history of diarrhea (60% vs. 30%), or 2 or more of the following symptoms: pneumonia, diarrhea, laryngitis (80% in HIV seropositives vs. 37% in HIV seronegatives). HIV seropositive children were also more likely to have had previous hospitalizations than HIV seronegative patients (40% vs. 12%). The 2 HIV seropositive children who died had a mean WBC of 3,800/mm^3 and a mean total lymphocyte count of 970/mm^3 which contrasted with counts of 10,600 and 3,800 respectively, in the 3 HIV seropositive children discharged with clinical improvement. Our final results in 300 children will demonstrate whether measles and HIV infection synergistically increase morbidity and mortality in African children.

THP.160 Detection of HIV Core Proteins in Biopsied Lymph Nodes from Patients with AIDS-Related Complex (ARC) and AIDS.

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Detection and localization of HIV (HTLV-III/LAV/ARV) antigen in the biopsied lymph nodes from patients with ARC and AIDS were studied by an avidin-biotin-complex (ABC) method using monoclonal antibodies (MoAb) against HIV core proteins p24, p17 and envelope protein gp 120. It was found that all MoAb were reactive with frozen lymph nodes of some patients, but the morphology of positive cells was poor. P24 and p17 were also detectable on formalin-fixed, paraffin embedded sections, and a stronger reaction was observed when we used MoAb p24. Eighteen biopsied lymph nodes from ARC patients and 2 from AIDS patients (both had Kaposi's sarcoma (KS) in the nodes) were the subjects for study of p24 on formalin-fixed, paraffin embedded sections. Of 13 lymph nodes which displayed follicular hyperplasia, 8 of them showed strong reaction, 3 of them weak reaction (or occasional cells being positive), and 2 of them were non-reactive. Five lymph nodes which displayed follicular regression and paracortical hyperplasia showed that four of them were reactive with p24 MoAb and one was negative. Lymph node biopsies from 2 patients with KS showed occasional cells being positive. Most positive cells were present in the follicular (germinal) centers, however, the interdigitating reticulum cells, histiocytes and endothelial cells were also positive in some instances. T-cell subsets (T4 and T8 cells) study was done in the same specimen (but from frozen lymph nodes) from seven patients. It was found that there was no correlation between the absolute counts of T4 and T8 cells in biopsied lymph nodes and the presence or absence of HIV core protein p24.

THP.161 Cytomegalovirus encephalitis in AIDS : an anatomo-clinical study of 4 cases.

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Post-mortem examination of 90 brains from AIDS patients provided evidence of CMV infection in 4(4.4%). Neurological symptoms and signs appeared 2 to 4 months before death. Early symptoms included behavioral changes, confusion, pyramidal tract signs and ataxia. At late stage, dementia, seizures, then coma developed. A mild CSF pleocytosis with protein ≥ 100 mg/dl was noted in 2 pts. In 3 cases CT showed cortical and subcortical atrophia. In one case CT was normal but MRI showed ventriculitis. At autopsy, gross pathologic findinds were a ventricular dilatation with peri-ventricular hemorrhage and a rough pattern of ventricular wall. Major histologic features were : small and large areas of polymorphic or histiolymphocytic cells with necrosis and microglial nodules. Inclusions typical of CMV were present in numerous cells within or without the inflammatory or necrosis foci. The major lesions were periventricular and/or disseminated in the white and gray matter. Cerebellum was also involved. In all cases immunoperoxidase staining proved conclusive for CMV, negative for HSV-1 and 2. HIV-RNA and proteins were not detected in 2 brains tested for. EM confirmed the diagnosis in all cases. CMV encephalitis was probably the results of overwhelming disseminated CMV infection in 2 pts, but not in the 2 others. These data suggest that subacute CMV encephalitis is not as rare as reported in AIDS.

THP.162 A COMPUTERISED NEUROPSYCMOLOGICAL BATTERY FOR THE ASSESSMENT OF HIV INFECTED ADULTS WITM EMPHASIS ON DETECTION OF EARLY CENTRAL NERVOUS SYSTEM INVOLVEMENT

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This paper presents a new and comprahensive psychomentric assesament battery for the detection and categorisation of the so-called AIDS Dementia Complex. The battery includes two seta of aenaitive computerized tests which even ill subjects find rewarding and interasting. Tha performance of standardised controls, asymptomatic HIV-positive, PGL, ARC, and AIDS groups were compared in two studies, the second of which ia the first staga of a two year longitudinal project.

Early results indicated impairment in those taska which demand more complex information processing and it is argued that early cantral nervous system involvement - the achievement of which is especially vital clinically - is most sensitively detected by using paradigma derived from experimantal work on Attention and Performance. The effectiveness of thia approach is illustrated using results from a computer adminiatered dual-attention task.

THP.163 Identification of Pneumocystis carinii (PC) in sputum; underestimation of cyst number with Giemsa.

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The diagnosis of PC pneumonia is currently based on morphologic recognition. The Giemsa stain demonstrates both the trophozoite and cyst forms. Its use has led to the impression that the trophozoite predominates in AIDS. This study was undertaken to determine which of several stains results in easiest recognition of PC, and to compare cyst number as seen by different stains. 16 dithiothreitol-liquefied PC-positive, frozen induced sputums were simultaneously thawed. Each sputum was vortexed and equally distributed onto 5 slides. The following 5 stains were done: (1) Giemsa; (2) toluidine blue; (3) silver methenamine; (4) toluidine blue/Giemsa; and (5) silver methenamine/Giemsa. Each slide was evaluated for number of recognizable units of PC at 10x, and number of cysts at 100x power. With stains (1),(4), and (5), the size of each PC aggregate was measured with an ocular micrometer. There was no difference among the stains in detectable number of units of PC organisms or amount of PC aggregate area. However, median number of cysts/sq.mm of PC aggregate area on Giemsa was 6.1 x 10^3 (range 0 - 11.5 x 10^3, interquartile interval 3.6-6.9 x 10^3), compared with 16.9 x 10^3 with toluidine blue/Giemsa (range 0 - 62.8 x 10^3, interquartile interval 7.7 - 45.4 x 10^3) and 6.7 x 10^3 with silver methenamine/Giemsa (range 0 - 57.6x10^3, interquartile interval 0.4 - 12.7 x 10^3). Cyst recognition with silver methenamine was hindered by the large amount of nonspecific silver staining. All the evaluated stains are equally suitable for diagnostic screening purposes. When accurate enumeration of cysts is important, the Giemsa stain, in comparison to toluidine blue, underestimates the number of cysts.

THP.164 Evaluation of Infectious and Immunologic Status by Bronchoalveolar Lavage in Patients with AIDS and ARC.

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Bronchoalveolar (BAL) was carried out in 17 AIDS and in 10 ARC with the aim of establishing an etiologic diagnosis of lung opportunist infection and to analyse the profile of immunocompetent alveolar cells.

In patients presenting with clinically and/or radiologically proven pneumonia, BAL revealed at least one opportunist pathogen in every case whereas it was negative in patients presenting neither clinical nor radiological signs of pneumonia. The analysis of the cells obtained by BAL showed that ARC group of patients presented hypercellularity (mean±SEM) : 295x103 C ±108x103 (ARC); 164x103 C ±29x103 (AIDS) (≤ 200x103 C in controls). Alveolar lymphocytosis was increased (AIDS : 26 ± 5.7%; ARC : 25.2 ± 7.4 %; ≤ 15 % in control) contrasting markedly with lymphopenia in the peripheral blood (AIDS : 33 ±7.2 cells(CD4) et 150 ± 40.8 cells(CD8); ARC : 271.7 ± 64.8 cells(CD4) et 436.7 ± 85.9 cells(CD8). Most of the alveolar lymphocytes expressed CD8 phenotypes whereas CD4 were severely depleted (CD4/CD8ratio : 0.16 (AIDS); 0,20 (ARC).

BAL appears to be an excellent mean for the diagnosis of lung infection but it also provides a new approach for studying the local immunity in the immunocompromised patients. We have undertaken a prospective study in asymptomatic HIV positive patient. The preliminary results in this third group suggest also modifications of the local immunity of the lung.

THP.165 Echocardiography detects cardiac involvement in Acquired Immunodeficiency Syndrome(AIDS): study in 70 patients.

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Little is known about cardiac involvement in AIDS.On that purpose 70 consecutive patients(pts)(mean age 29±7 sd years) 54(77%) males and 16(23%) females with AIDS diagnosed clinically and serologically were examined by means of TM and 2D Echocardiography with the aim of detecting cardiac abnormalities(C.A.).

64 Pts were affected by opportunistic infections,6 by Kaposi's sarcoma. No pt showed clear signs of heart failure. Results: 49/70(70%) pts showed C.A. characterized by left ventricle(LV) walls thickness(mean 8.3±0.2 mm),systolic thickening (mean 39±3 %) and particularly LV % shortening fraction(27±5) important reduction. 28/70(40%) Pts showed pericardial effusion,moderate in 23,cospicuous in 5. Moreover in 20 pts LV antero-apical dyssynergy and in 1 pt LV intracavitary mass was found. In 25 pts in clinically advanced state LV was globular and poorly contracting. 18 Pts died and necropsy showed in 12 pts globular shape of the heart,four chamber dilation,and LV walls thinning. Conclusion:despite little clinical suspicion C.A. in AIDS are frequent. An impairment in LV contractility appears to be the first Echo finding;followed by LV walls thinning,pericardial effusion and eventually by LV cavity dilation. This evolution is suggestive of myocardial damage induced by Human Immunodeficiency Virus.

Echocardiography proved very helpful in detection.

THP.166 Neopterin Levels Correlate with Walter Reed Staging Classification of HIV infection.

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In vitro and in vivo data contribute to the evidence that neopterin represents a sensitive marker for activation of macrophages by interferon-gamma. Due to the origin of interferon-gamma elevated neopterin is also characteristic for activation of T-cells. Since in vitro the production of HIV strictly depends on activation of T-cells there is a basis that neopterin might reflect the clinical state of HIV infection. To investigate the importance of neopterin in HIV infection 50 male subjects in different stages of the Walter Reed staging classification were repeatedly tested for neopterin levels in urine and serum over a three months period. Neopterin was measured in urine samples using HPLC standard techniques and in serum by using RIA. Urinary neopterin levels were related to creatinine. In addition, data from the medical history, physical examinations, whole blood cell count, blood chemistry, HIV serology, in vitro and in vivo tests for cellular immunity were collected.

Neopterin levels in urine and in serum showed a significant correlation with the Walter Reed staging classification. Neopterin levels in urine and serum rose with progression of the disease as measured by the WR classification.

THP.167 Flexible Fiberoptic Bronchoscopy and Bronchoalveolar Lavage (B.A.L.) for Diagnosis of Opportunistic Infections in Pediatric Patients with A.I.D.S.

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We report our experience with the technique of B.A.L. using flexible fiberoptic bronchoscopy in 10 children with A.I.D.S. Indication for the procedure was worsening in pulmonary status in patients previously diagnosed as having A.I.D.S., or evidence of interstitial pneumonia in patients with a presumptive diagnosis of opportunistic infection. From a total of 10 patients, four lavages were positive for Pneumocystis carinii; one was positive for Pneumocystis carinii and Pseudomonas Aeruginosa (cultures from B.A.L. and blood were also positive for Pseudomonas), and five lavages were negative. Pathological examination by way of autopsy in three patients correlated 100% with bronchoscopy findings. (positive for Pneumocystis carinii, positive for Pneumocystis carinii and Pseudomonas,and negative for opportunistic infection.) The most common complication was mild to moderate epistaxis in 3 patients; one patient required endotracheal intubation due to CO2 retention.

In the majority of cases, the pulmonary involvement in pediatric patients with A.I.D.S. is due to opportunistic infections or lymphocytic interatitial pneumonia. The flexible fiberoptic bronchoscopy with bronchoalveolar lavage offers an effective and relatively safe method for the diagnosis of opportunistic infections in this population of patients.

THP.168 HIV-Infection in a Cohort of Hemophiliacs

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780 hemophiliacs are treated at the Institute for experimental hematology, University of Bonn. Of these, 475 (61%) are infected with the Human Immunodeficiency Virus (HIV). The percentage of HIV-infection differs depending on the number of factor units the patients received.

164 HIV-infected hemophiliacs were seen as outpatients at the Medical Clinic,University of Bonn. 78 (47,5%)were symptomless carriers of the virus, 86 (52,5%) displayed symptoms of the HIV-infection, 27 of them having less than 100 $CD4^+$ lymphocytes/µl blood.

From 1982 through January 1987 15 hemophiliacs developped AIDS according to the CDC-criteria. 10 of them had their primary manifestation in 1986 or 1987. These were opportunistic infections in 10 patients, neurological manifestations in 5 patients, and malignancies in 2 patients (2 patients had more than one initial manifestation).

The 5 HIV-infected female sexual partners of hemophiliacs investigated so far are symptomless carriers at present.

Our data do not show any different natural history of HIV-infection in hemophiliacs as compared to other risk groups.

THP.169 Acute hepatitis during human immunodeficiency virus (HIV) primary infection.

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Acute hepatitis was observed in 7 adult patients (pts) (6 males, 1 female, aged from 23 to 41 years) among 15 well documented cases of HIV primary infection. All pts had fever with other symptoms and signs (sore throat : 6, rash : 7, meningitis : 3, adenopathies : 10, splenomegaly : 4, dysphagia : 3, diarrhea : 6). HIV primary infection was assessed by sequential serum ELISA and Western Blot. In the 7 pts with hepatitis, HIV was transmitted through sexual intercourse (5 pts) and direct parenteral exposure (2 pts). Transaminases raise was observed from 8 to 53 days after the onset of fever (mean ASAT peak : 8.8 x normal value). Mild cholestasis (Alkaline phosphatase : 2 x normal value) occurred in one pt. One pt was subicteric and non specific digestive symptoms were observed in five. Needle liver biopsy showed mild cytolysis with portal inflammation in 2. Liver function tests returned to normal within 10 weeks. In all pts other hepatitis agents were ruled out by negative virus isolation (CMV), negative antigenemia (HBV) and lack of IgM antibodies and/or seroconversion (HAV, CMV, EBV, HSV, Treponema, Toxoplasma) on repeated tests. Acute hepatitis seems common during HIV primary infection (46%). Although concomitant non A-non B virus infection cannot be definitively excluded, hepatitis might be due to HIV itself.

THP.170 Anti-D and anti-c immunoglobulin for HIV related thrombocytopenic purpura.

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The potential risks of steroids and splenectomy in HIV infected patients led us to evaluate the efficiency and safety of anti-D and anti-c immunoglobulin in 9 adults with HIV related thrombocytopenic purpura. They were 5 drug addicts and 4 homosexual men ; all had HIV antibodies but none had full blown AIDS. None were splenectomized. The platelet count was below $15 \times 10^9/l$ in all patients. The 7 Rh+ patients received 1,000 µg (12 to 20 µg/Kg) of anti-D IgG (Bio-Transfusion, France) intravenously on 2 consecutive days. The 2 Rh- patients were given an equivalent dose of anti-c IgG (20 ml of plasma from a single donor). A significant platelet rise above $50.10^9/l$ was obtained in 6 patients. Repeated boosters were efficient in 4 cases.

Direct antiglobulin test became positive in all patients and serial quantitative evaluations of IgG coating of red blood cells (RBC) were performed in 4. Only one patient experienced a significant hemoglobin drop. Eluates of platelet bound IgG were not modified by the therapy.

To further elucidate the mechanism of the therapy, two patients received consecutively both regimens : one Rh+ (C+, D+, E-, c-, e+) patient who responded to anti-D IgG received one course of the anti-c regimen without any significant response. One Rh- (C-, D-, E-, c+, e+) patient did not respond to anti-D but had a good response with anti-c IgG.

These data suggest that anti-Rh IgG can be efficient and safe in patients with HIV related thrombocytopenic purpura and that a specific interaction between RBC and anti-Rh antibodies is required.

THP.171 Mediastinoscopy and Mediastinal Lymphadenopathy in AIDS Patients. JIHAD SLIM, G.E. TONNESSEN, G. PEREZ, E. PEREZ E.S. JOHNSON. St. Michael's Medical Center, Newark, New Jersey.

A 16 month experience (8/85-12/86) involving mediastinoscopies in AIDS patients led to the following review.

In this period 10 procedures were done and all yielded diagnoses. Only one patient suffered any sequelae. All 10 patients had positive gallium scans prior to the procedure, 80% chest x-ray evidence and 90% CT scan evidence of adenopathy.

All the patients had bone marrow biopsies with no diagnoses and one non-diagnostic peripheral node biopsy.

All the results were infectious in origin with 20% showing cryptococcus (both with + serum crypt antigen) and 80% showing acid-fast bacilli. In the acid-fast group 3 of 8 were mycobacteria scrofulacium, 1 of 8 mycobacteria tuberculosis and 2 of 8 did not grow.

Except for one post operative mortality all clinically improved on therapy initially, but 6 of 9 eventually died with all still showing evidence of their original disease at the time of death.

These results suggest that mediastinoscopy is a safe valuable diagnostic procedure. Also infections are the primary causes of mediastinal lymphadenopathy with malignancy conspiculously absent.

THP.172 ALTERNATIVE SITE COUNSELLING AND HIV SCREENING. SM Burns, RP BRETTLE, C Bisset, J Davidson, S Davidson, JMN Gray et al. City Screening Clinic, Edinburgh, Scotland.

Extensive infection with Human Immunodeficiency Virus (HIV) amongst intravenous drug misusers (IDMs) ocurred in Edinburgh between 1983 and 1985. With the introduction of routine HIV screening of blood donations would current and ex IDM attend an alternative counselling and screening clinic outwith the Blood Transfusion Service and Sexually Transmitted Diseases service?

In one year from October 1985 - September 1986 441 individuals attended the City Screening Clinic (CSC) for counselling. There was a 35% default rate on the first appointment, a 21% post test default rate and a test refusal rate of 7% which ranged from 2.5% in IDMs, 3% in their sexual contacts, 7.5% in homosexuals, 9% in heterosexual contacts to 20% in those with no identified risk activity. Of those attending 43.5% were IDMs, 20% their sexual contacts, 12% heterosexual contacts in general, 9% homosexuals/bisexuals, 3% had been exposed to blood and 12.5% with no identified high risk activities.

The overall HIV seropositivity rate was 26%, 52% in IDM, 10% in homosexuals/bisexuals and 7% in sexual contacts of IDM. Despite initial sceptism there is a place for an alternative counselling and screening clinic on a site distinct from the Blood Transfusion and Sexually Transmitted Diseases services directed towards but not just for IDM.

THP.173 Lessons of History: How best can we buy time awaiting a vaccine for HIV?

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Recognizing that HIV is a sexually transmitted disease, we can gain some insights into the probable dynamics of the HIV epidemic by looking at syphilis information from the pre-antibiotic era.

In 1917, a survey using the Wasserman blood test in United States Army personnel showed a 16.77% positive rate overall, a 16.08% rate in white enlisted men, and a 36.0% rate in black enlisted men. Over the next 25 years, major efforts were made to reduce the prevalence of syphilis in the United States. Educational programs were launched to teach the population about human reproduction, the venereal diseases and how to avoid them. Prostitution was suppressed, and the case finding technique with medical treatment of positive contacts using Arsphenamine was developed. The effectiveness of this multipronged attack is seen in the Wasserman Blood Survey data of 2 million World War II recruits in 1941. The overall rate was 4.77%, with a white rate of 2.35% and a black rate of 27.2%. From this data we would drawn several conclusions: (a) That multiple efforts, including a modestly effective treatment, will reduce but not stop the spread of a sexually transmitted disease, thereby buying time for the development of a vaccine. (b) Minority groups require specialized programs with exceptional allocation of resources. (c) Massive crash educational programs will alert the general population to the danger of HIV, but a long term thoughtful multifaceted program will be required to significantly slow the spread of HIV.

THP.174 HIV Laboratory Reporting: The First 12 Months in Colorado FREDERICK C. WOLF, C. RAEVSKY, N. SPENCER, S. VALWAY, Colorado Department of Health, Denver, CO, U.S.A.

In November 1985, the Colorado State Board of Health required laboratories which collect or process specimens in Colorado to report individuals testing positive for HIV antigen or antibody to the Colorado Department of Health (CDH). The regulation was implemented in February 1986 by CDH staff visits to clinical laboratories. The controversial regulation which is similar to those for syphilis and gonorrhea, has been complied with.

In 1986, 391 reports were submitted (average 32.6 per month) by 38 laboratories (21 in Colorado and 17 in other states including commercial, federal, military, hospital and plasma laboratories). The number of reports by laboratory averaged 10.3 (range 1 to 75). Compliance is illustrated by completion rates for patient data (name, 94.6%, date of birth 69.8%, sex 92.1%, race 51.9%, address 67.5%), provider data (name 94.1%, address 70.9%), and laboratory data (name 98.0%, test date 79.0%, test type 93.1%, test result 91.6%).

Reported positives (391) were predominantly men (323, 82.6%), although 37 (9.5%) were women. Most (61.8%) reports were on persons between 20 and 34 years old. Patient name allows identification of repeat tests on individuals (391 positives on 363 individuals). Although number of tests processed is currently being collected, positive reports from these laboratories accounted for approximately 24% of all newly identified HIV Ab positive tests in Colorado during 1986. HIV laboratory reporting by name is a practical and essential program to understand the full scope of the HIV epidemic and trigger follow-up for prevention counseling.

THP.175 HIV Seropositivity in Newborns: A novel method for estimating prevalence of infection in childbearing women.

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As a prerequisite for designing programs to reduce perinatal transmission of HIV, we determined the rate of seropositivity at birth among Massachusetts infants of various demographic characteristics. Individual anonymity was assured by removing identifiers from the PKU (filter paper-adsorbed) blood specimens that were used for microassay of HIV antibody. Immunoblot was used to confirm an IgG-specific immunofluorescence assay that detected antibody primarily of maternal origin. Births from Dec'86 through Jan'87 provided 4919 specimens in three batches from groups of hospitals with the respective characteristics of "inner city", mixed metropolitan, and suburban/rural, and which represent about 45% of state-wide births.

	Inner City	Mixed Metro	Suburban and rural	Not tested	Totals
Annual births	5385	18,256	12,266	43,845	79,752
Number tested	849	2,499	1,571	-	4,919
HIV Ab(+)	13	8	2	-	23
(Rate/1000)	(15.3)	(3.2)	(1.3)	-	-

The concentration of seropositivity in inner city hospital births (15.3/1000) was not unexpected but the widespread distribution of rates between 1/1000 and 3/1000, and the assumption that 1/1000 was the minimal rate among hospitals not sampled, led us to a minimum estimate of 2.6/1000 as the state-wide average.

THP.176 A Model for Assessing Statewide Needs for HIV Prevention and Risk Reduction Education KAREN A. HECKERT, K.L. MACDONALD, R.N. DANILA, M.T. OSTERHOLM. Minnesota Department of Health, Minneapolis, MN, U.S.A.

The Association of State and Territorial Health Officers and the Centers for Disease Control have recommended the development of community education and risk reduction efforts to prevent transmission of Human Immunodeficiency Virus (HIV) in every state. The MN. Dept. of Health is implementing a comprehensive statewide risk reduction and disease prevention plan to identify, assess, and respond to professional, community, and client needs. This plan applies L. Green's health education planning model, PRECEDE, for determining appropriate educational strategies by collecting epidemiologic, social, behavioral, and educational data. Ongoing AIDS surveillance, HIV counseling and testing, and community programs serve to collect some of these data. We have also developed eight survey tools designed to collect information on knowledge, attitudes, risk behaviors, and availability of community resources from health-care providers, public health professionals and persons at high risk. These surveys include: 1,000 persons randomly selected from the general population, 500 gay-identified men, 300 intravenous drug users, 180 persons with hemophilia, 600 randomly selected family practitioners and internists, all 75 infection control practitioners in acute care facilities, 1,000 hospital nurses with potential exposure to HIV and all 73 public health nursing directors at local health departments. Implications for educational strategies for clinical providers, public health professionals and at risk clients are drawn from survey results and may have valuable application to other low prevalence states.

THP.177 Evaluation of an AIDS Education Unit for High School Students.
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We conducted a survey to assess the effects of an AIDS curriculum on high school students' knowledge and attitudes about AIDS. The survey contained 23 items and was administered to a population of 240 eleventh graders before and after instruction.

When scores were compared for percentage correct responses on knowledge items, scores following instruction were 16% higher. Significant changes were observed on most questions; e.g., students learned that kissing, giving blood and food handling are not major risk for AIDS transmission. Prior to instruction, 71% of students believed that sharing needles was a risky behavior compared to 92% after the class.

Attitude questions were grouped and scored on the basis of restrictive and fearful versus tolerant and compassionate beliefs about people with AIDS. A 15% increase in tolerance was observed following instruction, corresponding to the 16% increase in knowledge about AIDS. When asked prior to instruction where they learned about AIDS, only 30% of students mentioned school. Schools become the major source of learning (72%) after only one hour of instruction.

In conclusion, apparently even one hour of AIDS instruction can positively impact what young people know about AIDS. More importantly, knowledge appears to influence attitudes. This may enable an adolescent to make informed decisions about AIDS as a public health issue and to make safer choices in risk-taking behavior.

THP.178 Needle cleaning knowledge among intravenous drug users in treatment and AIDS prevention policy
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Proper sterilization of needles may be important in reducing HIV transmission among IV drug users. In a 1986 survey, 164 patients in a large New York City methadone maintenance program were asked what they thought was the "best way to clean needles." While 43 subjects (26%) said only that one should "always use new needles," 121 (73%) named at least one medically-accepted cleaning method. Among the latter, alcohol (64%)--the traditional method among IV users--and boiling (43%) were named most often; few (12%) knew about the recently promoted bleach method, and none knew about peroxide. However, being able to name a method does not always mean that subjects know how to use it correctly.

Gender, education, and minority status had no relationship with knowledge of at least one medically-recognized effective method (alcohol, boiling, bleach, peroxide). There were relationships with subjects' drug use patterns. The most likely to show needle-cleaning knowledge were the moderately-frequent injectors: those who, during the year preceding the interview, had continued to inject but on a less-than-daily basis. Similarly, those who last injected more than a month but less than two years before the interview were most likely to know how to sterilize needles. These moderately-frequent and moderately-recent injectors participate in both street-drug and treatment worlds and, while still injecting, may be particularly concerned with disease prevention.

Policy implications include: 1) the importance of needle-cleaning education efforts among frequent injectors, who have both the highest infection risk and the least cleaning knowledge; 2) the untapped educational outreach potential of the moderate injectors, who might be used as informal information conduits from treatment programs to street users.

THP.179 Sexual Behavior Change among HIV Seropositive Individuals.
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Sexual behavior was assessed in 95 HIV seropositive subjects enrolled in a prospective study of the natural history of AIDS to determine if there was significant sexual behavior change as a result of supportive counselling and education provided during the study. All 95 subjects (65 males, 30 females) were seen by the same investigator during the 12 month evaluation period and received the same intense one-on-one counselling and education regarding safe sex practices. The subjects were categorized into group (1) 46 homosexual men, group (11) 36 intravenous drug abusers (IVDA) and group (111) 13 blood transfusion recipients and heterosexual contacts. At entry and at each 3-monthly visit subjects were asked whether they had adopted each of 3 modifications.Data collected showed that 85% had fewer different sexual partners, 76% had adopted safe sex practices and 73% began condom use during sexual activity. Since enrollment 23% had not adopted any consistent modifications in their behavior. Overall sexual activity decreased significantly in all subgroups in terms of number of partners, specific high risk activities and failure to use condoms. The greatest change was seen in group 1 subjects and was more striking in males than females in each of the other subgroups. The least change was among IVDA prostitutes. Among 22 patients who failed to adopt any consistent modification, 7 developed STD's and 6 were involved in a pregnancy.

These findings suggest that ongoing counselling and education about AIDS leads to changes in sexual behavior among HIV infected persons.

THP.180 Analysis of Variables Impacting on Safe Sexual Behavior Among Homosexual Men in an Area of Low Incidence for AIDS
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In an effort to assess the impact of risk reduction education targeted at the male homosexual community in Northeastern Ohio, 303 men attending one of two homosexual social outings were studied in the fall of 1986 by means of a questionnaire describing their recent sexual practices as well as a number of variables including basic demographics, sources of information of safe sex, personal knowledge of their HIV serologic status, use of available medical resources and others. Among the respondants only 28% (Group-I) were practicing totally safe sex with 71% (Group-II) persisting in some activities that have been clearly described as unsafe. Among Group-II the vast majority admitted to some modification of their sexual behavior and 75% admitted to feeling comfortable that they have taken adequate sexual precautions. In addition, among those who had not been tested for HIV antibody (n=210) 95% predicted that they would be seronegative. Univariant and multivariant analysis comparing Group-I to the elicited variables revealed no association between safe sexual behavior and any of the elicited variables including knowledge of a friend with AIDS, personal knowledge of their serologic status, or receiving advice on AIDS from a physician. We conclude that educational efforts on safe sex education in our area have resulted in clinically meaningful behavior modification in only a small segment of the socially and sexually active homosexual community. Furthermore, additional studies are urgently needed to define the barriers to change so that clear and effective educational programs can be developed.

THP.181 Needs Assessment and Development of Model Standards for AIDS Primary Prevention in California
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Despite widespread discussion about AIDS prevention, no model standard or masterplan for primary prevention exists. To remedy this situation, the California Health Policy and Research Foundation and the Department of Health Services have developed a set of model standards for prevention that are responsive to needs and resources at the community level. These are based on recommendations of the 1986 Institute of Medicine Report and are informed by relevant prevention literature and expertise of California's public health, research and service provider communities. To establish a baseline of the state's prevention needs, we undertook site visits in five counties representative of a diverse range of geographic and population characteristics. Activities and information assessed included surveillance (case reporting for AIDS and ARC), seroprevalence data on general and specific populations, screening activities, educational interventions, skill building programs, drug abuse programs, special population activities, and program evaluations. In addition, we ascertained size, political and socioeconomic characteristics and location of at-risk populations and their accessibility for primary prevention interventions. We identified gaps between the proposed model standards and ongoing programs and made recommendations to narrow the gap.

We believe that both the model standards and the process of assessing local prevention needs are generalizeable to other state or regional prevention and planning efforts.

THP.182 A Comparison Of Three Educational Models For Changing AIDS Risk-Associated Behaviors
JOANNE MANTELL, ANTHONY DIVITTIS, LEE KOCHEMS, PETER MASTROIANNI, KEVIN MAHONY, CHARLES MCKINNEY

A community-based risk reduction program was conducted to test the relative effectiveness of three educational strategies in changing AIDS-related knowledge, attitudes, behavioral intentions and behaviors among a sample of 515 gay and bisexual men.

Men were randomly assigned to a cognitive-behavioral (CB), cognitive-affective (CA) or cognitive only (C) condition. The CB and CA curricula were six-session groups in which a didactic presentation about AIDS, its transmission and modes of protection were given, followed by a group process. The CB group process used skill-building behavioral techniques. The CA process focused on participants' emotional responses to the information. The C group received weekly mailings matched to the content of the other two strategies.

All groups completed a baseline screening instrument, a pre-test, and a post-test, at program completion and four-months later. The battery included self-report measures of knowledge and attitudes about AIDS, perceived susceptibility, self-efficacy, self-esteem, personal control, adequacy of supports, and risk-associated intentions and behaviors.

Preliminary analysis of the screening instrument indicated that of those participants who engage in anal sex, 36% rarely or never use a condom whether the active or passive partner (n=281; n=231, respectively). Of the participants who engage in either active or passive oral sex, 80% indicated that they rarely or never use a condom. Data regarding the relative effectiveness of each program based on pre-test and post-test 1 data are being analyzed, and will be presented.

THP.183 Statewide Free Condom Distribution Program
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Proper use of condoms are an effective method to prevent AIDS and other STD infections.

In an effort to make condoms available, the concept of "Three-For-Free" was developed by the Maryland State Department of Health and Mental Hygiene. The purpose of "Three-For-Free" is to decrease the number of barriers to condom use by making free condoms and instructions available for anonymous pick-up at as many sites as possible in Maryland. At most sites, bags of condoms and instructions are placed on tabletops in hallways, waiting rooms, bathrooms or clinic examination rooms. As of December 1986, "Three-For-Free" sites have been established in thirteen county health departments, five social service agencies, three Maryland universities, and eight clinics in Baltimore City. In less than one year, approximately 75,000 condoms with instructional pamphlets have been distributed through this program.

The State of Maryland also supplies free condoms to Baltimore City STD clinics. In order to increase the availability of condoms to risk groups in Maryland, the State Health Department supplies condoms at cost to a non-profit community agency for distribution to high risk groups.

An illustrated, wallet-sized pamphlet has been developed to be distributed along with the condoms.

THP.184 Street Outreach AIDS Prevention Program for IV Drug Users.
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Estimates indicate only 10% of IV Drug users are in treatment at any one time. In order to accomplish effective AIDS prevention among the 90% not in treatment, a program was designed to assimilate peer AIDS education outreach workers into known drug use communities in Baltimore City. Reformed IVDU's who had successfully undergone treatment were recruited and trained about AIDS, with specific emphasis on viral transmission, prevention guidelines, and communication skills. The workers were well-received, and pre- and post-intervention evaluations demonstrated a significantly increased awareness among targeted IVDU's not in treatment programs.

Success of the program depended on careful selection of outreach workers. Successful candidates were identifed by scores on a rating scale incorporating factors such as drug abusing history, length of time in treatment, treatment progress, reading and educational level, interpersonal skills and motivation level. Team building and organizational support were identified as significant components in outreach workers' abilities to cope with job-related stress, including return to drug use.

THP.185 Motivations and Consequences of AIDS Antibody Testing Among Heterosexuals. SUSAN KEGELES, JOSEPH CATANIA, AND THOMAS J. COATES, University of California, San Francisco, School of Medicine.

This study was designed to determine demographic characteristics of heterosexuals seeking antibody testing, to assess why heterosexuals seek antibody testing, to obtain data on measures of susceptibility and anxiety specific to AIDS, and to determine consequences of antibody testing. Data on 232 respondents were collected at two antibody testing centers in Alameda County, California; 40.5% (n=124) were heterosexuals. Respondents were administered questionnaires when they arrived at the testing sites, and were followed at 1 and 6 months post-testing. Approximately 65% of heterosexuals had sought antibody testing because of concerns that they may have contracted HIV from sexual contacts; approximately 20% had sought testing becsuse of concerns they were IV drug users, with the remainder being concerned because of transfusions (10%) for miscellaneous reasons (5%). Approximately 26% of the males and 32% of the females were continuing to engage in high risk sexual activities in the month prior to obtaining antibody testing. Perception of increased susceptibility for AIDS were associated with greater anxiety over the possibility of developing AIDS. However, male heterosexuals (even when seeking testing) perceived themselves as less susceptible to contracting HIV than male homosexuals. Antibody postive status was associated with reductions in high risk behavior than antibody negative status.

THP.186 Voluntary Screening For HIV Infection In Patients Attending A Sexually Transmitted Diseases Clinic
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To determine the prevalence of HIV infection in persons attending a Sexually Transmitted Diseases (STD) clinic and in order to offer counselling and voluntary partner referral, we instituted a program offering voluntary, anonymous serologic testing of all persons attending the STD clinic. We continued serologic testing by request at the STD clinic and at New Mexico AIDS Services (NMAS). Serum was screened by EIA, and sera positive by EIA were confirmed by indirect flourescent antibody testing. 693 of 1221 patients (52% of 155 gay males, 57% of 662 heterosexual males, and 58% of 404 females) seen from October 1 to December 31, 1986 accepted the test, and 12 (1.7%) were positive. All 12 were gay males. In contrast, 16 (9.8%) of 163 screened by request at the STD clinic, and 12 (11.7%) of 102 screened at NMAS were seropositive. Of 265 screened by request, 21 were screened for symptoms and 14 because of exposure to a seropositive partner. Twelve (86%) of these 14 were seronegative. We conclude that voluntary, anonymous HIV screening is accepted by both heterosexual and homosexual patients attending a STD clinic. Knowledge that a partner was seropositive led to screening and counselling in 5.2% of persons requesting screening, and 86% of these were seronegative at the time of counselling. Voluntary screening of persons attending STD clinics and voluntary partner referral should be considered in areas of low seroprevalence for HIV antibody.

THP.187 Teaching AIDS: A Resource for High School AIDS Prevention Programs
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The need for resources for high school AIDS prevention programs has been noted by many policy experts. The first professionally published, nationally distributed curriculum for high school students represents an important contribution in this area. The curriculum includes rationales for teaching AIDS to high school students, basic information about AIDS, suggestions for and concerns of teachers, and seven teaching plans. The plsns are appropriste for a variety of classes, including family life, science, history, social studies, civics or psychology.

THP.188 The Centers for Disease Control (CDC) Computerized Bibliography for Information on the Acquired Immunodeficiency Syndrome (AIDS)
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There has been an explosive increase in the number of requests for AIDS information received by CDC. In the last 2 months of 1986, the Technical Information Activity office of the AIDS Program, Center for Infectious Diseases at CDC filled 670 requests for journal reprints, responded to 362 letters, and answered 17 telephone calls per day (average). Many more such inquiries are received by other CDC offices. Inquiries come from State and local health agencies, infection control practitioners, clinicians, counselors, Federal and State legislators, a multitude of grass-roots AIDS organizations, and many others seeking to educate themselves or care for others. Quick access to relevant information is necessary to assist these people in accomplishing their work.

One source used to assess what CDC personnel have written on AIDS is the computerized bibliographic retrieval system. One of the databases maintained on this system includes published articles written by CDC staff members on prevention, public health policy, epidemiology, surveillance, and laboratory research. The database also includes 94 AIDS-related articles published in the Morbidity and Mortality Weekly Report. The bibliography can be requested through the Information Resources Management Office, or it can be accessed through any terminal linked to the main CDC computer. Searches can be requested by various parameters (e.g. subject, author, time period, journal).

New software for this database will provide easier access and wider application. The new system will be one of the most efficient mechanisms for public health workers, clinicians, and others to document CDC AIDS-related information and respond to important demands.

THP.189 HIV Antibody Testing in British Columbia: An 18-month Report
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HIV antibody testing has been available in British Columbia since October 7, 1985. An ELISA test is used initially with IFA and Western Blot confirmation. Testing is available through any registered physician and through a government testing, evaluation and counselling clinic in Vancouver. The laboratory requisition notes age, sex, date, risk group, physician and geographic location. Results of over 10,000 tests have shown the following prevalences: gay/bisexual males 25%, intravenous drug users 3%, heterosexual contacts 1%, hemophiliacs 28%, blood transfusion recipients 1%, and prostitutes 2%. The overall reactivity rate was 10%. Samples submitted per month were stable at 400-500 until 1987 when the number began to rise dramatically. Accompanying the rise in samples submitted the monthly reactivity rate declined from 12-15% to less than 3%. Private physicians submit approximately 60% of all samples followed by hospitals (16%) and the government clinic (15%). Samples from the government clinic have a significantly lower reactivity rate than those from elsewhere, perhaps reflecting a reluctance for those at greatest risk to use the government facility.

This testing system has proven acceptable to the medical community, to high risk groups and to the general public. The results have been useful to public health officials.

THP.190 Strategies for Intervention in Minority Communities
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The incidence of STDs among adolescents suggest that the future rate of HIV infection may far exceed its present rate. Data on Black adolescents strongly suggest that they may be at increased risk of HIV infection. A survey of misconceptions about AIDS indicates that Black and Hispanic adolescents were twice as likely than White adolescents to believe that AIDS could be contracted through casual contact, i.e., touching or being near someone with AIDS ($p<.01$). Black and Hispanic adolescents were also more likely to believe that "all gay men have AIDS" ($p<.01$) and that "all gay women have AIDS" ($p<.001$). These findings suggest that adolescents generalize from gay men to gay women even though there is no evidence to suggest that this group is at risk of HIV infection. These misconceptions may increase adolescents, particularly Black and Hispanic adolescents' risk of HIV infection by diverting attention from risk behaviors. To dispel these misconceptions requires communicating factual information about AIDS and sensitivity to the cultural and emotional issues which the AIDS epidemic engenders. This requires a systematic public health education effort including school-based AIDS curricula as well as the support and participation of the community-at-large. One strategy may be to train indigenous community members/groups to serve as educational resources, as they may be sensitive to potential barriers that could inhibit receptivity to AIDS information and behavior change. Interventions in minority communities will be discussed.

THP.191 The impact of information on AIDS: The blood donor perspective
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Since 1983 all donors receive information on AIDS and risk factors by circular letter, and since May 1985 on anti-HIV testing. A study was set up to investigate: 1) Adequacy of information, 2) How donors associate with the information and 3) Impact of information on motivation.

Methods: Analysis of donor population in period '83-'87, and a postal questionnaire sent to a random sample (500) of the donor population (55,000).

Results: 133 persons (115m/18f) terminated blood donation indicating a risk factor. Total donor population increased 7%, without any change in demographic composition. The increase did not differ from previous years. From the 133 'risk factor' donors, 18 (13.7%) enrolled as a first time donor. These 18 represent only 0.12% of all first time donors registered since April '83. Of over 97,000 donations tested since May '85 only 4 (0.004%) were confirmed positive (W8 +IF). The results of the questionnaire showed positive attitude, good motivation of the donor population and great concern with information on AIDS. However, results show striking discrepancies between aspects of attitude, and cognitive aspects.

Conclusion: Combining test results and results of the self-deferral programme it seems that the given information was well received by those who recognise a link with risk factors. In contrast, the results of the postal survey indicate that to the majority of our donor population the right emphasis and meaning are not adequately conveyed by the given information.

THP.192 Random-digit Telephone Survey for Knowledge and Attitude about AIDS
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Trained interviewers, using a random-digit dialing system, called 3,650 Vermont phone numbers state-wide soliciting both knowledge and attitudes about AIDS and HIV transmission. Interviews were completed on 602 Vermont residents aged 18 and older. Responses were analyzed by demographic variables, including age, sex and education. Thirty-one questions on the questionnaire which had clear answers were chosen to test the knowledge of those surveyed.

Persons with greater education, those who were younger and the male gender tended to answer more questions correctly. Questions answered more correctly by all respondents included those concerned with risks associated with sharing needles (96% correct), male homosexual sex (96% correct) and heterosexual sex (94% correct). Ninety-five per cent of the respondents correctly stated that persons can be infected with the AIDS virus without their knowledge.

Questions that tended to be answered incorrectly included those concerning the lack of risk associated with female homosexual sex (10% correct) and potential risk of virus transmission through breast milk (26% correct). Only 75% of respondents stated that you could not catch AIDS from donating blood. Those surveyed had inconsistent responses on the lack of risk of casual transmission. Ninety-five per cent stated one could not catch AIDS by shaking hands; but only 64% stated that AIDS could not be transmitted through sharing a drinking glass or an eating utensil. Whereas 78% of respondents felt that it was all right for children with the AIDS virus to attend school, only 60% would not be worried about their child catching AIDS from a classmate.

Those surveyed seemed to be knowledgeable about the major risks for infection but less knowledgeable about the lack of risk of casual transmission.

THP.193 Anonymous Testing in Public Places: A Social Psychological Examination of the Destigmitization of HIV Antibody Testing
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A team of social psychologists and public health AIDS program staff designed and implemented the first freely accessible and anonymous testing offered to the general public apart from the alternate test sites. During a two day health fair conducted in the busy lobby of the Federal Building in Cincinnati and at the work site of an Environmental Protection Agency, 225 individuals completed questionnaires examining attitudes about AIDS and 84 individuals requested HIV testing. Destigmitization of the test was achieved by positioning it between diabetes and blood pressure screening.

This presentation considers issues related to the social psychology of AIDS antibody testing and the factors that need to be considered in the destigmitization of the test.

AIDS hysteria is described as a form of collective behavior in which the public finds itself in an ill defined normative setting. Routine, anonymous, and wellness-oriented HIV screening is presented as a means of resolving ambiguity and decreasing AIDS hysteria.

THP.194 The Level of Knowledge and Attitudes Regarding AIDS and HIV Infection in the Nashville, Tennessee Metropolitan Area
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A survey was conducted of the adult Nashville, Tennessee Metropolitan population during September, 1986 to establish the level of knowledge and types of attitudes concerning AIDS and HIV infection. The instrument was developed on the basis of previous studies; it included 8 demographic questions, 22 knowledge-base questions, and 4 attitudinal questions. Subjects were randomly chosen from the area phonebook and surveyed by trained interviewers.

Four-hundred and five subjects participated. Comparison of demographics with census reports indicated the sample to be representative; in particular level of education and racial figures were highly representative.

Three results were considered significant both statistically and for program development in AIDS education and prevention. First, demographic variables statistically associated with the highest level of knowledge about AIDS were general level of education and age. The more educated the subject, the more he or she knew about AIDS; younger subjects knew more about AIDS than older subjects. Second, the difference in level of knowledge about AIDS between blacks and whites was so slight statistically that it posed no practical implications. And third, a strong statistical association existed between higher levels of knowledge about AIDS and a resistance to sanction employment and housing discrimination against persons infected with HIV. This result supports the importance of general AIDS education programs.

AIDS education and prevention programs in metropolitan areas with lower caseloads can be assisted in their development by studies of existing local attitudes and levels of knowledge concerning AIDS.

THP.195 AIDS and Biomedical Research: A Comparative Analysis

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The rapidly expanding AIDS research budget may be exacerbating political pressures to reduce or slow the rate of growth in biomedical research funding aimed at other health impairments. In this paper, we present a framework and method for comparing the size of the AIDS research budget to the size of research budget for Cancer, Coronary Heart Disease (CHD), and Accidents. The framework utilizes information about several measures of the burden of health impairments on society; deaths, early deaths, forgone life years, and medical care costs. The calculations in the paper relate Fiscal Year 1986 budgetary expenditures to projection of disease burden in 1991.

We show that these four health impairments are not given equal investment priorities by the Federal Government. Accidents receive relatively little priority; Cancer and AIDS are roughly comparable. The priority assigned to CHD is sensitive to the index of disease burden selected by the analyst. The paper relates these findings to the National Research Council's recent recommendation of one billion dollars AIDS research budget for 1990. The authors of the paper urge policy makers and scientific institutions to make explicit decisions about the marginal productivity of research investments - against health impairments - that claim limited resources.

THP.196 An Ethnography of Needle Sharing

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The hypodermic set ("works") has a meaning in the heroin subculture beyond that of a mechanism to achieve a goal. It is a symbolic representation of the world of dope.

Sharing and reusing works among IV drug users is a significant means for transmission of the HIV. Street wisdom often dictates behaviors that foster continued transmission. For example, addicts have learned that boiling the works jams the plunger by removing the silicon lubricant. However, much street wisdom has little factual foundation, rather serving only socialization processes.

The care and maintenance of works serves to perpetuate reuse, as do users' perceptions of statutes that restrict sale and possession. HIV is transmitted at the shooting gallery, but users' perception of the latter is complex. A few galleries provide only rental of works. More sell drugs, only secondarily renting works. Still more provide free access to works for drug purchasers. Many house dealers allow steady customers to borrow works as a convenience. Finally, some users become known for their willingness to allow friends to shoot up in their homes.

Along this continuum, the risk for HIV transmission is a function of the number of users involved in sharing and the looseness of the participant network. An understanding of user perceptions and behavior is crucial to the development of prevention efforts directed toward reducing the spread of the virus through these sharing processes.

THP.197 The effect of AIDS diagnosis upon close personal interactions among family members of AIDS patients.

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To explore the effect of AIDS diagnosis upon behavior, we evaluated the sharing of household facilities and items and close personal interactions among household contacts of AIDS patients before and after the diagnosis of AIDS and during two time periods in which availability of information about risk of household transmission differed.

199 household contacts of AIDS patients were evaluated with detailed standardized interviews to determine the nature and amount of household interactions with the AIDS patient. The first 104 (group 1) were evaluated from 10/84 to 5/85, the second 95 (group 2) from 6/85 to 11/86, after information about lack of transmission of HIV infection was known and made available to study participants. The median age of the 2 groups was similar. Of the 199, 144 had household contact both before and after the AIDS diagnosis (87 in group 1, 57 in group 2).

By McNemar's test for matched pairs, significant decreases in sharing of household items occurred after diagnosis in both groups: combs, towels, eating utensils, plates, glasses. In group 1 measures of close personal interaction decreased significantly after diagnosis: (hugging 78-54%, kissing 86-67%). In the group 2 there was no significant change in these close personal interactions after diagnosis (hugging 70-63%, kissing 65-61%).

Despite information showing lack of risk of transmission among household members of AIDS patients, significant reduction in sharing of household items and facilities occurred. Close personal interactions were maintained, however, after information about lack of risk became available. Therefore, Patients and family interactions may be influenced by information about lack of transmission.

THP.198 Beliefs and Behaviors Regarding AIDS: A Survey of Street Intravenous Drug Users.

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Effective work in helping addicts to engage in risk reduction behaviors will be enhanced by understanding what addicts currently believe about AIDS, and what their relevant behaviors are. Data were collected by a "street survey" of addicts in one high-drug-use area in each of three New York City boroughs. While most previous reports have studied IV users in treatment programs, street users are particularly important as a group that continues frequent IV drug use. The Street Research Unit of the New York State Division of Substance Abuse Services asked open-ended questions of 137 IV drug users who were unaware that they were being interviewed.

Three quarters of these "street addicts" knew that the spread of the AIDS virus is related to IV drug use and four-fifths relate it to sexual activity. The proportion aware of drug use as a factor is noticeably lower than that reported for a 1984 sample of methadone maintenance treatment clients (Friedman & Des Jarlais, 1986). Slightly over half of the street IV drug users engage in at least one valid protective measure, very similar to Friedman & Des Jarlais' comparable proportion. Two-fifths have changed their drug taking practices to protect themselves, while measures related to sex were mentioned by one fifth. These findings show that although there is already considerable knowledge and risk reduction even by street addicts, there are also large numbers who lack information and/or sufficient motivation to engage in risk reduction behaviors. Efforts to disseminate accurate information about AIDS to street IV users are likely to result in an increase in both knowedge and risk reduction practices.

THP.199 Accurate Determination of Risk Behavior in Persons with AIDS.

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The New York City Department of Health AIDS Surveillance conducts sensitive investigation of AIDS patients denying major risk factors of intravenous drug use (IVDU), male homosexuality, transfusion and, for women, sex with a man at risk. Of 270 cases reported monthly, 19 (7%) fail to identify a risk on initial interview. After investigation, 40% of these cases are found to have engaged in IVDU or homosexuality. Of 204 women claiming sex with a man at risk, all knew their sex partners were at risk and could identify them by name. Sixty (29%) were married or common-law to the man. Nineteen (9%) were later identified to be IVDU themselves. Only four (8%) of 53 males claiming female contact were able to identify the women they believed infected them. Three men claiming sex with Haitian women as a sole risk had engaged in homosexual activity. Of 47 men claiming sex with female prostitutes, 31 (66%) had engaged in IVDU or homosexuality. Seven of eight health care workers claiming occupational exposure were subsequently identified as IVDU or homosexuals. Our statistics support the epidemiologic benefit of careful case investigation.

Interview of AIDS patients or close contacts is psychologically stressful for interviewer and interviewee. Supportative elicitation of highly personal information can represent a catharsis for the individual, who may have significant motives for denial of risk behavior. This paper addresses issues encountered in undertaking investigations. Case material provides examples of how to initiate, sustain, make transistions and close a non-identified risk interview while maintaining the utmost concern for the patient's feelings, rights and dignity.

THP.200 A Model of Psychosocial Intervention in a Family Practice Center: for persons with Human Immunodeficiency Virus

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The Family Practice Center (FPC) of Meharry Medical College has developed a model of psychosocial intervention for patients with Aquired Immune Deficiency Syndrome (AIDS) and other Human Immunodeficiency Virus (HIV) related conditions.

The patients served by the center are typically socially and economically disadvantaged with minimal social support and limited access to medical care.

All patients diagnosed or suspected being at high risk for AIDS are evaluated by a trained AIDS counselor using a twenty-two page Inventory Assessment Form. Individualized comprehensive treatment plans are then developed to provide patients with emotional, social, medical and economic assistance.

In evaluating these patients, it has been found that they and their lovers, family members and friends are severely stressed. Even persons who are antibody-negative but athigh risk for infection are found to exhibit symptoms indicative of stress.

Recurrent psychological themes found are depression, conflict associated with a life threatening illness, feelings of isolation from friends, family and medical personnel, guilt, diminished self-esteem, preoccupation with economic problems and suicidal thoughts.

Our experience, following one year of intervention, suggests that individual and group counseling enhances the quality of life for these patients and augments the effectiveness of the medical care delivered.

THP.201 Homelessness in Patients with the Acquired Immune Deficiency Syndrome (AIDS).

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The number of homeless individuals in New York City (NYC) increased from approximately 7,500 to 10,000 from 1/85 to 12/86. Since North Central Bronx Hospital(NCB) serves one of NYC's poorest boroughs, we tried to determine if homelessness was a major problem among our AIDS patients and, if so, how it affected their discharge planning.

From 9/85 to 9/86, 87 patients with full-blown AIDS were hospitalized at NCB. Seventy-seven were intravenous drug abusers (IVDA) or their sexual partners; 10 were homosexual. Seventy-eight were members of minority groups. Seventy-two (83%) either lived with relatives (68) or had their own homes (4). Fifteen (17%) were homeless; 14/15 were IVDA; 10/15 (66%) were homeless prior to the diagnosis of AIDS. Of the 15 homeless patients, 4 were accepted home by relatives or friends; 4 went to hotel rooms provided by the municipal social services department; 3 went to hospices; 3 died; 1 left against medical advice.

Although largely IVDAs from indigent minority groups, the majority (83%) of our AIDS patients had family or friends who accepted them within their homes despite their diagnosis. Homelessness is still a problem for a significant number of our AIDS patients (17%) who often have severe social problems unrelated to their diagnosis of AIDS. Discharge planning thus becomes more difficult.

THP.202 Attitudes of Female Prostitutes in London to Barrier Protection.
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Fifty-two female prostitutes were recruited to the anthropological component of a prospective study of STD and lifestyle at the Praed Street Clinic between 7.86 and 1.87.

Female prostitutes are placed in a high risk category for HIV infection but condoms are thought to offer significant protection. Research on the epidemiology and the effectiveness of condoms will have to be considered in terms of their use. Data collected so far suggest:-

1. London prostitutes are predisposed to use barrier protection in order to avoid contamination with semen itself, as well as possible infection. The entire sample used condoms some of the time with clients at the time of their first visit.
2. This population is also predisposed not to use barrier protection with non-paying partners, including pimps. The discrimination provides a critical means of demarcating work from pleasure, and 'punters' from 'partners'.
3. The women in this group are worried about affecting other prostitutes. This anxiety is related to common ideas about prostitutes as individual sources of infection and a collective pool of infection.

Health education has been able to capitalise on two of these conclusions and the amount of condom use with clients has risen. However, there has been little change in patterns of use with non-paying partners. As this latter group is said to have contact with many other women, this may be a critical avenue for infection.

THP.203 Psychological Interventions for Persons With AIDS and Their Partners: A Group Approach.
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In this report from the University of California AIDS Health Project, the author will present a group model for working with homosexual and heterosexual couples in which at least one of the partners is diagnosed with AIDS. The author will present case material based upon eight completed groups involving a total of 33 couples. Couples were either self-referred or referred by mental health practitioners. The primary psychological themes presented by each individual and the impact of these issues on the couple will be addressed. The goals of the group include: 1. increasing coping and adaptive skills, 2. increasing independent functioning of the individual and couple, 3. improving communication skills and 4. augmenting social support. Group interventions for medically ill populations including patients with coronary disease, cancer and other life-threatening illnesses have been extensively documented in the literature, as has the impact of the illness on the family. The author will discuss the relevance of this literature in work with this population.

THP.204

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THP.205 The Right-to-Know: AIDS-Free International Certificates.
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HIV infection has presented modern medicine with novel challenges and e thical dilemmas demanding innovation if its spread is to be controlled within the framework of a free and responsible society. Infected people usually remain infectious, unknowingly, for several years before illness ensues, and they are particularly likely to infect wives, husbands, fiances and infants. People who are not infected with HIV have a Right-to-Know. They also have a Right-to-Know that another person with whom they are proposing to start, or continue, a sexual relationship - whether within or outside marriage - is also not infected. All "safe sex" techniques are inconsistent with procreation.

The serological tests used to screen blood prior to transfusion provide very good evidence of freedom from infection with HIV. This information on a certificate would satisfy the Right-to-Know of individuals and their sexual partners. The certificate must be unforgeable, up-datable, internationally recognisable and clearly identifyable as belonging to the owner. Only laboratories approved by public health authorities and WHO should be licensed to test. Active encouragement by governments, WHO, medical, scientific and religious leaders for people to obtain certificates on a voluntary basis will benefit individuals and slow transmission of the virus in the community. The need for the certificates to be regularly up-dated will provide a powerful incentive for responsible behaviour - particularly by young people.

THP.206 Medicine in Plague Time: Duty or Virtue? ABIGAIL ZUGER and S.H. MILES, Center for Clinical Medical Ethics, Department of Medicine, University of Chicago Hospitals and Clinics, Chicago, Illinois.

The profound reluctance of some physicians to care for patients with AIDS prompted us to review medical responses to analogous historical plagues. No consistent professional tradition emerged. Many historical physicians, including Galen and Sydenham, fled from patients with contagious epidemic diseases. Many of their colleagues remained behind to care for plague victims at considerable personal risk. No formal statement of this duty, however, was enunciated until 1847. This historical ambivalence suggests that an ethic stressing traditional professional duties may not be ideal for defining the optimal relation of the medical profession to patients with AIDS.

A new statement to guide the profession in the AIDS pandemic cannot invoke punitive sanctions against physicians refusing to treat HIV-infected persons, for these would violate physicians' civil liberties and personal autonomy. Nor can it be derived from these patients' right to health care, for that is a claim against society rather than individual practitioners. Civil and professional proscriptions against negligence or abandonment apply only to therapeutic liaisons after they are contracted. However, a professional duty to treat HIV-infected persons could be based on the understanding of medicine as a moral enterprise. In this context, treating HIV-infected persons is a virtuous act, that meets both patients' and society's health needs and confirms the moral mission of health care.

THP.207 Management of Confidentiality by a Cohort of Gay and Bisexual Men Who have Learned their Antibody Status.
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While much attention has been given to the issue of confidentiality within the research process, there has been little recognition of the difficulties those who are undergoing HIV antibody testing may have in maintaining their own privacy once they leave the research setting. We followed, for an average 10 months, 116 gay and bisexual men who were tested for HIV antibody as part of ongoing epidemiologic studies conducted by the Health Department and the Centers for Disease Control. Of those who chose to learn their antibody status, both seropositives (N=51) and seronegatives (N=36) told an average of 19 of their acquaintances their serostatus. Those who chose not to learn their antibody status (N=29) told fewer acquaintances ($\bar{X}$=14) about their having been tested and their decision not to find out the results. Several of those interviewed noted changes in relationships, either for the better or for the worse, that they attribute to risk status disclosure. Few, however, would change whom they told about their risk status had they the opportunity to reconsider these past decisions. Likewise, if they could choose anew, nearly all stated that they would consent to being tested again as part of the research process.

Study participants found disclosure of antibody or risk status to others to be either helpful or neither helpful or harmful. In general, these men have not encountered damaging reactions to disclosure of antibody status in the relatively supportive environment of San Francisco.

THP.208 Continuous Variables, Discrete Decisions: Determination of Ethically Acceptable Risks of False Laboratory Results in Blood Donor Screening.
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The establishment of appropriate "cut-offs" for screening assays in blood banks raises issues that go beyond the technical, medical and scientific community and require the resolution of ethical issues. The problem occurs because: (1) sophisticated assays produce continuous results, e.g. the ELISA for antibodies to HIV produces results from zero to maximum, may miss specific antibodies and detects non-specific antibodies; the cut-off value that separates reactives from non-reactives is arbitrarily defined as the best possible discriminator between populations and presumably normal individuals, and (2) assay results have to be applied without the benefit of clinical evaluations combining medical history, physical examination and laboratory studies. The problem is further complicated by unrealistic expectations of no risk of disease transmission by transfusion, goal that can only be achieved by eliminating transfusions.

Risk-benefit assessment can be used in the determination of screening assay cut-offs. Committees comprised of experts, ethicists and recipients could, at regular intervals, determine the maximum acceptable risk for a transmissible disease based on epidemiologic studies, clinical trials, assay characteristics, and curves of risk probability of various cut-offs. Recipients of transfusion would be able to make their own decision based on this information. Insurance carriers would have guidelines for coverage, and the legal system would have means for dealing with litigation and compensation of victims.

THP.209 Issues of Foster Care and HIV Infection in Infants of Drug Addicted Mothers.
ANN SUNDERLAND*, H. MENDEZ*, S. HOLMAN*, M. BERTHAUD*, G. MOROSO*, S. LANDESMAN*, et al. SUNY Health Science Center at Brooklyn**, Brooklyn, N.Y., U.S.A.and National Institutes of Health**, Bethesda, M.D., U.S.A.

A cohort of 43 babies born to HIV seropositive (SP) and seronegative(SN) drug addicted (DA) women are being followed in a prospective perinatal HIV transmission study. Sixteen of 43 (36.1%) of these are in foster care (FC). There is no difference in incidence of placement between SP(9/16) and SN(7/16) groups. Where results are known to the FC system, 3/4 SP babies are in group settings as foster homes are unavailable, including 1 "boarder baby" awaiting placement out of the hospital and 1 child who was abandoned by the caretaker after learning results.

Placement of babies tested for HIV raises ethical dilemmas involving confidentiality. A mothers right of confidentiality conflicts with a caretakers right to know results. The latter is needed for proper precautions and appropriate delivery of health care. Informing a FC agency of the serological status of a child born to a SP mother may jeopardize or limit placement possibilities. As fear of AIDS may hinder placement of all babies born to DA women, telling results may enhance SN baby's chance of placement. Informed consent obtained when testing the mother should allow for informing the FC system of the baby's status.

Our experience and the estimate of 800-1000 SP infants born in N.Y.C. per year points to the need for the FC agencies and their governmental overseers to (1) develop a coherent policy for educating case workers, and potential foster care parents and (2) increase recruitment efforts for foster parents of SP infants.

THP.210 American Corporate Policy on AIDS and Employment
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Survey was sent to "Fortune 1000" companies in October and again in November, 1986 in order to learn approaches of America's major corporations towards employees with AIDS and related conditions. Of 165 companies which responded non-anonymously, 165 (100%) indicated they provide health insurance benefits to employees with AIDS or ARC, 164 (99.5%) indicated that they do not test employees or job applicants for HIV antibodies, 109 (66%) declared that it is their official policy to forbid employment discrimination against employees with AIDS or related conditions, and 38 (23%) had developed or are developing written policies on AIDS. In addition, several companies indicated that they have provided educational materials and programs about AIDS to their employees.

Results are significant because they reveal higher-than-previously-estimated degree of proactive response by major employers to the AIDS epidemic. It is hoped that survey findings will encourage other employers, as well as government agencies, to develop compassionate, legally sound policies towards employees and applicants with AIDS and related conditions without fearing that they will be going out on a limb to do so.

THP.211

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THP.212 HIV Seroprevalence Among Nurses Caring for Children with AIDS/ARC
MARY BOLAND, J. KERESZTES, P. EVANS, J. OLESKE, E. CONNOR
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Sera from 45 female nurses caring for children with AIDS/ARC at CHNJ was tested for HIV antibody. The nurses were volunteers who anonymously completed a questionnaire designed to define type of patient contact and to identify HIV infection risk factors. Nurses worked in the following areas: ICU (14); medical-surgical units (26); ambulatory service (2), and AIDS program (3). 26 (56%) of the nurses cared for patients for over 12 months for an average of 8-12 hour shifts/month (0-15 shifts). Nurses reported the following types of contact: bathing (41/45), feeding (41/45), care of central venous catheters (42/45), administration of oral and intravenous medication (40/45), obtaining and handling specimens (e.g. blood, urine, stool) (45/45), contact with blood and secretions (eg diaper changes) (43/45) and touching and comforting a child (43/45).

The nurses reported following standard hospital infection control procedures sometimes 4 (9%), usually 25 (25%), and always 15 (32%). 3/45 nurses reported needlesticks and 2/45 reported mucous membrane or broken skin contact with a child's blood. 43/45 nurses were healthy. 1/45 had the diagnosis of chronic Esptein Barr Virus infection; 1/45 had contact dermatitis of the hand that required periodic use of steroid cream. 3/45 had received blood transfusions within the past 5 years. All denied nonprescription drug use and all were heterosexual. 1/45 had a sexual partner who since developed AIDS, and 1/45 reported a present partner who is HIV positive.

100% (45/45) nurses were HIV negative by ELISA and Western Blot. Annual re-testing is ongoing. Data from this study suggests that risk of transmission of HIV during nursing care of children with AIDS/ARC appears to be small.

THP.213 Attitudes Concerning AIDS: Relationship to Behaviors of Dental Health Professionals

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To determine AIDS patients' access to dental care, a randomized survey of dental health professionals in California was conducted. Respondents' attitudes, knowledge, and behaviors regarding patients with AIDS and at-risk for AIDS were assessed, as well as the number of patients they perceived to be at-risk for AIDS in their practice. Usable responses were obtained from 297 dentists, 128 hygienists, and 177 dental assistants. Use of infection control was more closely related to attitudes than to knowledge in all three professional groups. When compared with practitioners who thought few of their patients were at-risk for AIDS, those who perceived more of their patients to be at risk had more positive attitudes ($p<.004$) and were more likely to practice infection control ($p<.0001$) and to screen patients for AIDS by taking a thorough medical history ($p<.02$) and sexual history ($p<.04$). The authors conclude that attitudes toward AIDS, particularly perception of the number of patients at risk in one's practice, affect the screening and infection control procedures used by dental health professionals. Attitudes, rather than knowledge, should be targeted in education programs designed to improve AIDS patients' access to dental care.

THP.214 Creation of a Dedicated Unit for AIDS & HIV-Related Illness (HIV Patients) at Bellevue Hospital- Impact on ICU Utilization, Care Patterns of Critical Patients & Mortality

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A designated unit (12E) for HIV patients with 10 private rooms was created in January, 1986 to concentrate nursing care for acutely ill, non-intubated patients and provide an alternative to ICU for these patients. We studied the 278 admissions during the 6 months prior to the opening of 12E ('Pre') and the 298 admissions during the 6 months following it's opening ('Post'). During this period the average daily census of HIV patients was 46.6 (range 37-55). 133 admissions were excluded because they spanned the transition period.

The proportion of HIV admissions who spent time in ICU, 15%, and the mean length of stay (LOS) in ICU, 7.5 days, did not differ significantly between the two periods. Mortality of ICU admissions was 53.5% during both periods compared to 30% for 12E admissions and 20% for all HIV admissions. Mean LOS in the ICU for patients who died was 10 days in contrast to 4.7 days for those who survived. Mean LOS on 12E was 8.6 for patients who died and 12.4 for those who survived. It is notable that the LOS of patients in ICU who died is longer than that of those who lived while the reverse is true for 12E. This may be attributable to the fact that patients in respiratory distress who elected not to be intubated were often admitted to 12E where their deaths were not prolonged by mechanical ventilation.

We conclude that the creation of a dedicated unit did not alter ICU utilization or overall mortality for HIV patients. Instead, it offered a setting in which acutely ill, non-intubated patients could receive a higher level of nursing care. This relieved the burden experienced by the general medical wards and provided a humane alternative for critically ill patients who chose not to undergo intensive care.

THP.215 Absence of HIV Antibody Among Dental Professionals, Surgeons, and Household Contacts Exposed to Persons with HIV Infection.

SCOTT HARPER, N. FLYNN, J. VAN HORNE, S. JAIN, J. CARLSON, S. POLLET, et al. Univ. of California, Davis, Sacramento, CA.

Dental professionals and surgeons have increased risk of acquiring hepatitis B through professional contact with this virus, raising the question of transmission (T) of HIV in the same manner. Close household contacts of HIV-infected individuals (HIV-I) have not been shown to be at risk for T of HIV.

To examine these hypotheses we tested 300 Sacramento and L.A., CA dentists, hygienists, and chairside assistants (who experienced approximately 200 or more exposures to HIV-I), 25 surgeons who operated on HIV-I (usually unaware of HIV infection) and 20 household contacts of HIV-I, for antibodies to HIV by ELISA and Western blot techniques. An additional 700 dentists from major U.S. cities will be tested prior to presentation of this data. Subjects were asked not to participate if they had any other recognized risk factor(s) for HIV exposure. We also questioned dental professionals regarding gloving practices and frequency of accidental puncture wounds. Dentists and chairsides seldom wore gloves, whereas hygienists wore them for the majority of procedures. 42% reported ≥2 puncture wounds per month, 25% had ≥6 per month.

No subject had antibody to HIV by Western blot analysis. We conclude that risk of T of HIV to dental professionals in Sacramento is small. Our small numbers of surgeons and household contacts provide additional evidence that T of HIV in these settings is rare.

THP.216 Hepatitis Delta Antigenemia in Intravenous Drug Abusers with AIDS: Potential Risk for Health Care Workers

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Intravenous drug abusers (DA) are the second largest group at risk for infection with HIV and developing AIDS (25% of U.S. cases). DA are also a major risk group for infection with hepatitis B virus (HBV); over 80% of heroin addicts have some marker of HBV infection. Hepatitis delta virus (HDV) is a defective RNA virus which can replicate only in the presence of replicating HBV. The prevalence of HDV infection, which can cause fulminant hepatitis and death, or rapid progression to cirrhosis, has been increasing in DA. This study was conducted to determine the prevalance of markers of HDV infection along with HBV markers in a group of unselected DA entering or in treatment and, in a group of DA with AIDS disease and to examine the relationship of immunosuppression in AIDS on the expression of HDV infection.

	Subjects(N)	Positive Test:	HB$_s$Ag	HDAg	anti-HDV
PDA	347		18 (5.2%)	2 (0.6%)	104 (30.0%)
PDA with AIDS	53		8 (15.1%)	3 (5.7%)	0 (0%)

The overall prevalence of HDV markers was 27.3% in DA subjects. Delta antigenemia, associated with infectivity, and usually detected only in the first 2 weeks of delta infection, was found in a significantly increased number of DA with AIDS, probably due to either a persistence or reappearance of antigen in the setting of AIDS related immunosuppression. HBV vaccination to protect against HBV and HDV infection is recommended for all persons working with blood from patients with HIV disease.

THP.217 Coming Home Hospice: A Model Residential Hospice Alternative

JEANNEE PARKER MARTIN, Director, AIDS Home Care and Hospice Program, San Francisco, CA.

In 1984, Hospice of San Francisco developed the first AIDS Home Care and Hospice Program in the country. This program has provided care for more than 500 AIDS/ARC patients at home.

Increasingly, needs for 24-hour attendant care and supervision have been identified. Consolidated housing alternatives were established to help meet this need but were inadequate.

In March 1987, Hospice of San Francisco will open Coming Home Hospice, a residential board and care facility for terminally ill persons with AIDS and ARC. This facility will allow 15 patients to receive comprehensive hospice services 24 hours a day. These services will be provided by Licensed Vocational Nurses, attendants, volunteers, Registered Nurses, and Social Workers.

This presentation will highlight the unique characteristics of Coming Home Hospice, its Advisory Board, community support, and public and private funding sources.

THP.218 A Model for AIDS Professional Education

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A model has been developed specific to the education of physicians and nurses, in practice and in-training, at the University of California, San Francisco. Over a 3-year period, under federal contract, 5000 health practitioners will be comprehensively educated via this model.

Curricula have been fashioned with sensitivity for HIV-related diseases as medical illnesses, as the topic of extensive research, and as diseases of unprecedented psychosocial and legal/ethical complexities. The model extends beyond traditional educational frameworks; it addresses the dilemma of how to impart both technical and provocative information in such a way that it is not only assimilated but applied. An emphasis on diagnosis and treatment is matched by that placed upon prevention and health education.

The numerous organizational challenges of AIDS professional education are reflected in this model; attention has been paid to interdisciplinary issues and related concerns about professional domain, interagency cooperation, and the integration of community issues into the academic arena. In keeping with epidemiologic trends, both curricula and core faculty reflect the special concerns of third world persons, substance abusers, recipients of blood products, women and children.

THP.219 Identifying Major Concerns of Patients with AIDS

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A descriptive study was conducted to identify and categorize major concerns of individuals with AIDS. Thirty adults were interviewed. The majority were male homosexuals with Kaposi sarcoma undergoing experimental therapies. Information gathered included impact of the diagnosis, major concerns, support networks, and persons and actions perceived most helpful.

The majority (66%) were told the diagnosis by a physician in person, and (30%) were told over the telephone. The most common reaction was shock or disbelief but 13% expressed relief and 7% expressed feeling "empty" or "dead". Eighty-three percent initially discussed their diagnosis with a lover or friend, while 10% first told a family member(s) with 77% responding in a manner perceived to be helpful. Helpfulness was described most frequently as keeping the relationship intact without significant change. The predominant concern expressed was personal health and continued functioning followed by uncertainty about the future, fear of death and completing research requirements. At the time of the interview 47% reported feeling always hopeful and 10% never hopeful. Ninety-seven percent reported some uncertainty, 90% fear, 90% fatigue, 97% sadness and 83% anger. Seventy-seven percent of the patients reported never feeling abandoned. From participation in research 23% hoped for a cure, 23% a treatment or experimental drug, and 23% maintenance or prolongation of function. Twenty percent expected no help for themselves but participated to help others.

Study information also provides understanding that gives direction to the planning and provision of quality care to this patient population.

THP.220 MULTIDISCIPLINARY APPROACH TO AIDS PATIENTS, POLICIES AND PROCEDURES IN A COMMUNITY HOSPITAL.

L. Andrews, R.N., S. Patronik, R.N., K. Hryb, B. Cooper, M.D., J.J. Klimek, M.D., Hartford Hospital, Hartford, CT, USA.

Ours is a 1,000 bed community teaching hospital in central CT where 1 to 4 new AIDS cases are treated each month. In response to increasing needs within our hospital, a Multidisciplinary Committee (MC) was formed to address patient care and staff issues.

MC is comprised of representatives from Epidemiology, Social Service, Nursing, Home Care, Pastoral Services, Microbiology, and Rehabilitation. MC functions as an educational resource, and attempts to identify and anticipate problems and share solutions. Members are notified of the admission of an AIDS patient, confidentially, in writing by the Section of Epidemiology. Bimonthly meetings are held during which issues are discussed, policies are established, and individual patient cases are reviewed. Specific patient problems and their solutions are addressed by a team with representatives from each discipline. Educational needs within the hospital are met through inservices to all departments on a regular basis.

The MC functions in conjunction with the Infection Control Committee and the Hospital Administration to anticipate and identify the needs of our institution. Collaboration with other state hospitals allows further sharing of problems and solutions.

As our number of AIDS admissions increases, this collaborative approach utilizing a variety of departments has worked well. This committee was comprised solely of representatives from within our institution and did not require additional funds or outside resources. The MC model may be useful for handling small to moderate numbers of AIDS admissions in a community setting, where resources are limited.

THP.221 Costs of AIDS to a Public Hospital.

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Since all AIDS cost studies have been based on patient charges rather than true hospital costs, and since public hospitals have fixed budgets, this study intends to determine the marginal costs of AIDS to PMH. From 1982-86, 168 persons with AIDS were admitted to PMH, accounting for a total of 252 admissions.* The number of admissions increased from 5 in 1982 to 134 in 1986. The total charges were $37,312 in 1982 and rose to $1.45 million in 1986. Marginal costs were determined by adding the cost components for labor (nursing, housestaff, and social work), ancillary services, dietary, pharmaceuticals, supplies, and laboratory. Estimates for nursing labor were based on standard patient care units assigned to each patient and for housestaff labor on progress note frequency. Total inpatient costs rose from $15,000 in 1982 to $1.03 million in 1986. The costs per admission peaked in 1984 and then declined due to a shorter mean length of stay: the mean stay was 22 days in 1984 and 12 days in 1986. The mean daily charge declined from $1,109 in 1984 to $872 in 1986. However the mean daily cost rose from $579 in 1984 to $719 in 1986. 14% of charges to AIDS patients were paid, compared to 31% of charges to other patients. AIDS has a substantial impact on the economics of public hospitals that requires major efforts at economic and epidemic forecasting to adapt the tax base to increasing case loads.

*1986 data are estimates pending final analysis.

THP.222 The Nurse Role in an HIV Diagnosis and Management Centre

Patrick M. Turbitt, Andrew Morlet, Julian Gold, Albion Street (AIDS) Centre, Sydney Hospital, N.S.W., Australia.

The Sydney AIDS clinic was established by the state government in March 1985 to provide free, confidential testing and management for persons infected with HIV. Over 6,000 people have presented for testing of whom 750 were HIV antibody positive. All HIV antibody positive persons are offered ongoing medical management, receive psychological assessment and counselling and return to the clinic for further T-cell testing and review every three to six months after initial diagnosis.

The nurse role in this context has developed to include the assessment of new clients to triage them into medium/high and low risk categories according to their likelihood of infection. The nurse collects demographic and extensive lifestyle data from those in the moderate/high risk group before referring for medical examination and counselling. The low risk persons are managed by nurses without referral.

Nursing staff are the first line contact for all clients entering the clinic, thus providing an important role in imparting factual, comprehensible information to allay fears and educate those who perceive themselves to be at risk. Nurses are also called upon to provide information to other health care professionals and to conduct in-service training.

Whilst the majority of HIV antibody positive clients are at the early stages of infection and require minimal clinical management, the nursing staff offer advice on maximising health, prevention of concurrent infection and reinforce safe sex practices.

THP.223 Update: Prospective Evaluation of Health-Care Workers Parenterally Exposed to Blood of Patients Infected with Human Immunodeficiency Virus.

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As of September 15, 1986, 1,116 health-care workers (HCWs) with documented exposures to blood of human immunodeficiency virus (HIV)-infected patients were enrolled in a surveillance project to determine the risk of occupationally acquiring HIV infection. HCWs have been followed for a mean of 20.7 months. Percutaneous exposures to blood accounted for 77% (n=856) of the incidents. Exposed HCWs included 679 nurses, 186 physicians, 111 laboratory workers, 68 phlebotomists, and 72 others. Exposures occurred in patient-care wards (59%), intensive-care units (20%), operating rooms and morgues (10%), laboratories (7%), and emergency rooms (4%). Exposures judged preventable included recapping used needles (17%), improperly disposing of used needles (13%), and contaminating open wounds (10%). HIV-antibody testing has been performed on serum samples from 716 (64%) exposed HCWs. Two hundred five HCWs with both acute-(≤30 days postexposure) and convalescent- phase (>90 days postexposure) serum samples tested for antibody to HIV were exposed to patients who meet the Centers for Disease Control's surveillance definition of AIDS; one (0.5%) has shown evidence of seroconversion. An additional 47 HCWs with paired serum samples were exposed to HIV-infected patients that did not meet the CDC definition of AIDS; none of these have seroconverted. We conclude that 1) at least 40% of injuries in this project might have been prevented by use of recommended infection control measures; 2) the risk (0.5%) of occupational transmission of HIV infection from patients with AIDS (CDC surveillance definition) is low (95% CI 0.00-2.30); and 3) the risk of infection from other HIV-infected patients warrants further examination.

THP.224 AIDS-HIV Education for Medical, Nursing, and Pharmacy Students at the UCSF School of Medicine

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Health care provider students may be thrust into clinical interactions with HIV-infected patients prior to receiving education on HIV and AIDS. This may lead to unecessary infection control behaviors and phobias of patients with AIDS and ARC. This may be true especially at UCSF because San Francisco has the highest density of AIDS cases of any U.S. city. In order to obviate this problem, a multidisciplinary survey elective course was designed and named, "AIDS-HIV 1987: Overview and Update." The course was modeled after a similar experimental course chaired by this author in the Spring quarter of 1986. A needs assessment of medical students, course evaluation forms from the Spring course, and input from various UCSF AIDS researchers and clinicians led to the curriculum design.

The Course is thirteen hours in length, including eleven lecture hours and 2 hours of panel discussions. Lecturers include nineteen UCSF AIDS researchers and clinicians. The Course lecture topics are: "Overview and Introduction;" "Epidemic Perspectives and Treatment Issues;" "Immunology, Lab Tests, and Autoimmunity;" "Virology and Vaccine Horizons;" "Clinical Manifestations of AIDS;" "ARC;" "Neurologic Manifestations;" "Oral Manifestations" "Transfusion and Blood Banking;" "Pediatric Manifestations;" "Hemophiliacs and AIDS;" "Psychiatric/Psychosocial Issues;" "Women and AIDS;" "Ethnic Minorities and AIDS;" "Infection Control;" "Health Care Provider Issues;" "Legal Issues;" "Public Policy;" and "Ethics." The two panels include: "Persons with AIDS and ARC;" and "San Francisco Systems of Care." Pre- and post-course knowledge and attitude questionnaires will be used to assess the success of the Course. The Spring Course led to decreased phobias and increased knowledge on HIV.

THP.225

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THP.226 Immunologic Reconstitution in AIDS Employing 3'-azido-3' deoxythymidine and Syngeneic Bone Marrow Transplantation

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The immunologic defect in AIDS is characterized by a decrease in the absolute number of helper/inducer T lymphocytes and an inability of the remaining cells to proliferate in vitro in response to soluble protein antigens. Bone marrow transplantation and the adoptive transfer of syngeneic lymphocytes employing identical twin pairs where one has AIDS and the other is HIV negative have accomplished only a transient improvement in immunologic function, presumably due to the destruction of the new immune system by HIV. The present study was designed to determine the effects of combining anti-retroviral therapy with 3'azido-3'deoxythymidine (AZT) with adoptive immunotherapy and bone marrow transplantation. Patients were selected for the study if they were culture positive for HIV (with or without clinical illness), demonstrated immunologic defects characteristic of HIV infection and had an identical twin with a normal immunologic profile and no evidence of HIV infection. Patients were treated with 500mg AZT q4h for the 12 weeks prior to bone marrow transplantation. At week 10 of AZT they received 4 infusions of peripheral blood lymphocytes from their identical twin, at week 12 of AZT they received 2 infusions of peripheral blood lymphocytes from their twin and at the end of week 12 they received the bone marrow transplant without conditioning. Following transplantation patients were randomized to receive either 100mg AZT or placebo q4h. At the present time 12 patients have entered the study and 4 bone marrow transplants have been performed. While it is still too early to assess the effects of this therapy it is hoped that the data generated over the next 4 months will allow an evaluation of the efficacy of anti-retroviral therapy with bone marrow transplantation in patients with HIV infection.

THP.227 Suramin-Imuthiol Combination Therapy of Patients with AIDS-Related Complex (ARC) Results in 6 cases

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Previous studies have shown us that suramin, despite its effectiveness as a HIV inhibitor, is unable to improve the immune and clinical status of patients with AIDS or ARC. We therefore started with a clinical trial combining suramin with diethyldithiocarbamate (Imuthiol) a drug with immunoregulatory properties in 6 patients with ARC. They all had initially lymphocyte cultures positive for HIV markers (HIV antigens and/or RT activity). Once the cultures became negative, suramin 1g IV every 2 weeks together with Imuthiol 10 mg/kg per os once weekly were administered for at least 16 weeks. Each patient was examined clinically and questioned for side-effects of drugs. Plasma suramin levels were determined by HPLC before each new administration of suramin.

The immune status of the patients was screened every 2 months for lymphocyte subsets and for cutaneous delayed hypersensitivity with 7 recall antigens (Multitest).

After 16 weeks of treatment, despite maintenance of plasma suramin levels $\geq 100 \mu g/ml$, there was no change of the clinical status of the patients and no improvement of % or absolute nb of T4 cells or skin tests score was observed.

One patient develop ed adrenal insufficiency.

THP.228 Ansamycin (Rifabutin), an Inhibitor of HIV in vitro, Crosses the Blood-Brain Barrier

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Current data indicate early involvement of the central nervous system by HIV; progressive encephalomyelopathy (HIV-EM) appears to be an exceedingly frequent complication of late HIV infections. The ultimate utility of candidate virustatic agents will probably depend on their ability to traverse the blood-brain barrier. Ansamycin (ANSA) (Rifabutin, LM427, spiropiperidyl rifamycin), a semisynthetic derivative of rifamycin S, inhibits HIV in vitro at concentrations greater than 5-10 micrograms/ml. ANSA was employed in an open-label clinical trial involving subjects with case-defined AIDS or HIV-EM, to determine toxicities and potential utility at doses greater than those employed for treatment of M. avium-intracellulare infections. Sera "spiked" with ANSA and its major 25-desacetylated metabolite, LM565, were heated to inactivate HIV (56°C, 20-30 min) without affecting drug detectability by high-pressure liquid chromatography (HPLC). Sera collected serially and CSF obtained after several weeks' oral dosing (300-600 mg/day) were assayed using a modification of an HPLC method established by Adria Laboratories. Both ANSA and LM565 were present in sera, but only ANSA was found in CSF, at levels 30-40% of those in serum. These studies indicate that ANSA traverses the blood-brain barrier, across clinically uninflamed meninges, fulfilling an essential requirement for drugs considered for the treatment of HIV infections.

THP.229 Open Trial of Azidothymidine (AZT) in AIDS Patients at Parkland Memorial Hospital (PMH), Dallas, Texas

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Forty patients have been enrolled in an open, uncontrolled trial of AZT at the AIDS Clinic (PMH). Of the 40 enrolled, there have been 7 deaths. Two deaths occurred during the week treatment was to have begun and 5 died during the first 3 weeks of therapy. Deaths were due to opportunistic infection or neurological deterioration. Six patients developed opportunistic infections diagnosed after at least 6 weeks on AZT. Three patients developed Pneumocystis carinii pneumonia and the other 3 have been diagnosed with Mycobacterium avium-intracellulare infection. One patient dropped out of the study because of intractable nausea and vomiting and another was lost to follow-up. The remaining 25 patients taking AZT are either clinically stable or improved. Of 20 patients taking AZT for a least 1 month, there has been an average weight gain of 4 lbs.

Side effects have been numerous and include nausea and vomiting in seven. Six of these seven improved after lowering the dose. Maculopapular/follicular skin reashes were seen in 5 patients. Two patients developed convulsions on the drug. Laboratory abnormalities have included unexplained, significant drops in the hemoglobin level of 4 patients who have required intermittent transfusions. Six patients had decreases in granulocyte counts requiring dosage adjustment, including one patient whose count fell soon after the initiation of acyclovir therapy. AZT represents a significant advance in AIDS therapy, but its administration is not without problems.

THP.230 Progressive Histopathology and Prognostic Value of Sequential Lymph Node Biopsies in Patients with AIDS and ARC.

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The prognostic value of progressive lymph node histopathology was studied in 66 sequential lymph node biopsies (bxs) from 27 male patients (2 to 6 bxs per patient) with the Acquired Immunodeficiency Syndrome (AIDS) or AIDS-related complex (ARC). Initial bxs revealed four patterns: explosive follicular hyperplasia (EFH) in 17; mixed EFH and follicular involution (M) in 5; follicular involution (FI) in 4; and lymphoid depletion (LD) in 1. Lymph node histology showed a progressive loss of follicles and lymphocytes corresponding to a temporal pattern of change; EFH to M to FI to LD. Overall 18 of 27 patients (67%) progressed to different histologies on repeat biopsy. On second bx of those 5 initially with M, 3 progressed; 2 to FI and 1 to LD. On the second bx of those 4 initially with FI, 3 progressed; 1 to LD and 2 to lymphoma. This progressive histologic pattern of change correlated with a deteriorating clinical course; there was an increased incidence of developing opportunistic infections (OI), Kaposi's sarcoma (KS), and lymphoma (L) and decreased mean time of survival. Of the 18 patients with progressive lymph node histology 15 died (83%). Of patients with FI or LD on first or second bx, 92% had or developed OI, KS, or L and died with a mean survival of 11.5 months. However, only 50% of those with EFH or M on first or second bx had these diseases and died, mean survival of 29.8 months (p=0.01). Sequential lymph node biopsies may be prognostic of the clinical course in AIDS and ARC.

THP.231 Successful Chemoprophylaxis for Pneumocystis carinii pneumonia with Dapsone in Patients with AIDS and ARC

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In an open study to evaluate the efficacy of dapsone for the prevention of Pneumocystis carinii pneumonia (PCP), we studied 156 patients who were at high risk for PCP from 4/85 to 1/87. The groups included patients with a prior history of PCP, other life-threatening opportunistic infections (OI), AIDS-related Kaposi's sarcoma (KS), generalized lymphadenopathy, ITP, and malignant lymphomas. All patients initially had less than 200 T4+ cells/mm^3. Only 1 patient receiving 25 mg po qid of dapsone developed PCP. This patient was also receiving ansamycin for disseminated MAI. Since ansamycin is a derivative of rifamycin and rifamycin lowers serum dapsone levels 7 to 10 fold, it is possible that ansamycin may have similarly affected dapsone levels. In contrast, 14 of 19 patients who refused treatment with dapsone and who were clinically matched with patients in this study developed PCP. Dapsone administration led to a decline in red cell mass, a rise in serum LDH, and the development of methemoglobinemia. 39 patients required one or more transfusions of packed red blood cells. However, temporary discontinuation of dapsone in 11 patients decreased the transfusion requirement but did not eliminate the need for repeated transfusions. Complications included nausea (2) and skin rash (6). Eight patients with ARC or AIDS developed KS while receiving dapsone. By itself, dapsone did not cause significant regression of any skin lesions and did not prevent the development of new lesions. 55 patients developed other life-threatening OI's or malignant complications; 36 of these patients have died. In summary, dapsone is well tolerated and highly effective in the prevention of PCP.

THP.232 Long-term Follow-up of Fansidar Prophylaxis for Pneumocystis carinii Pneumonia (PCP) in Patients With AIDS.

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PCP continues to be the most common opportunistic infection diagnosed in AIDS patients. While therapy with either trimethoprim-sulfamethoxazole (T/S) or pentamidine is successful in 80 to 90% of episodes of PCP, recurrence rates without prophylaxis remain between 30-50%/year. An increased prevalence of adverse reactions to T/S among AIDS patients often complicate use of this agent as prophylaxis for PCP.

We report 11 month (range 2.5-27) follow-up of 60 patients recovered from an initial episode of PCP given Fansidar (20:1 sulfadoxine+pyrimethamine) dosed 1 tablet/week. While 50/60 patients experienced adverse reactions to T/S (rash, leukopenia or GI disturbance) only 6/50 developed rash on Fansidar. No episodes of Stevens-Johnson syndrome were observed. Bronchoscopy with TB biopsy was done in 12/60 patients due to respiratory symptoms. PCP was diagnosed in 5/12 but not found in 7/12 (2 KS, 2 bacterial, 2 CMV, 1 no etiology). Plasma sulfonamide levels done in 3/5 patients with recurrent PCP were undetectable. No hematologic, hepatic or renal toxicity was noted in any patients.

We conclude that Fansidar prophylaxis significantly reduces the recurrence of PCP in AIDS patients and appears to be well-tolerated in the majority of patients with previous adverse reactions to T/S.

THP.233 An Antiviral Trial of Rifabutin in Patients with ARC.

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We are evaluating rifabutin (ansamycin, Adria Labs), a rifamycin S derivative, as a therapeutic agent for HIV infection in patients with ARC. Rifabutin was selected as a candidate drug for this phase I-II study because it inhibits HIV replication in vitro, enters the central nervous system (B. P. Davidson et al abstract this meeting), has minimal toxicity in AIDS patients treated with low doses for M. avium complex, and is taken orally.

We are treating HIV culture positive ARC patients with escalating doses of rifabutin. Virologic response is measured by monthly co-cultivation of patient peripheral mononuclear cells (PMCs) with normal donor PMCs. A significant increase in the time interval to positive reverse transcriptase activity post-treatment compared to pre-treatment is interpreted as a decrease in circulating HIV titer. We have treated 5 patients with a low daily dose of 450 mg and have followed them for 6-12 weeks clinically, immunologically and virologically. None of the patients treated at this initial dose showed any toxicity or change in clinical, immunologic or virologic status, but the serum levels at 450 mg are below the in vitro effective doses. We have therefore recently increased the dose to 600 mg daily on the 2 patients who showed no antiviral effects at 8 weeks (patients were cultured at 4 and 8 weeks). We have entered 5 new patients at 600 mg and are continuing the study. Groups of 5 new patients will be entered at escalating doses. The dose for each group of 5 new patients will be raised by 150 mg until antiviral or toxic effects are seen. In addition, if no antiviral effect is seen after a patient receives 8 weeks of therapy at a given dose, the dose will be escalated in the same manner.

THP.234 Effects of 3'-Azido-3'-deoxythymidine (AZT) in Patients with Acquired Immune Deficiency Syndrome (AIDS) post-pneumocystis carinii pneumonia infection.

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AZT has been shown to limit multiplication of HIV through inhibition of reverse transcriptase. A clinical trial using AZT 200 mg every 4 hours p.o. was initiated in 43 evaluable patients with AIDS post-pneumocystis carinii pneumonia (PCP) infection. Twelve concurrent opportunistic infections or tumor, i.e. CMV retinitis, Kaposi's sarcoma, cryptosporidiosis, candida esophagitis, mycobacterium avium intracellulare and Burkitt's lymphoma were present in some cases but did not require treatment while patients were receiving AZT. Median age was 33 years with median performance status of Karnofsky scale 90. All patients had 1 episode of PCP except 4 who had 2 episodes of PCP prior to starting treatment. The main side-effect was anemia which occurred in 30% of the patients and 26% required blood transfusion. Other side-effects included nausea, headache, fatigue, anxiety, confusion and skin rash. Treatment was interrupted in 19 patients due to hematologic toxicity, opportunistic infection, other infection and other medical problems. Twelve patients were treated for recurrent or possible recurrent PCP. Four patients refused further treatment due to intolerable gastrointestinal symptoms and fatigue. Clinical improvements were observed in the form of weight gain, decrease in abnormal liver function tests, increase in Hb and increased energy after taking AZT from 2 to 10 weeks. AZT may have a role in the treatment of AIDS patients with PCP.

THP.235 Improvement of Lymphoid Interstitial Pneumonitis in a Child Treated with Azidothmidine

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A seven year old girl with ALL in prolonged remission developed generalized lymphadenopathy, Strep. pneumoniae septicemia, and bilateral pulmonary infiltrates three years after she had received blood products from 23 donors. Antibody to HIV was present by ELISA and Western blot. She had hypergammaglobulinemia, cutaneous anergy, markedly low T4/T8 ratio and low total T4 number. IgG antibody to EBV capsid antigen was extremely high (1:4096) as was EBV early antigen (1:512). Her chest x-ray showed diffuse fine nodular opacities throughout both lungs and bilateral hilar adenopathy. Pulmonary function testing showed marked restrictive changes, however, blood gases were within normal limits. Open lung biopsy demonstrated severe chronic inflammation, mainly lymphocytes, in the perivascular, peribronchial, and interstitial regions and lymphoid follicles with germinal centers. No pathogens were demonstrated by routine or special stains. The child received 7 1/2 weeks of azidothymidine intravenously; at no point did she receive other antiviral or immunomodulator therapy. Physical examination, chest x-ray and pulmonary function tests all showed marked improvement in her lung disease. Her lymphadenopathy and splenomegaly also improved during IV therapy. Blood and CSF cultures for HIV, both initially positive, showed distinctly less RT activity during IV AZT; immunologic parameters did not change significantly during the initial study period. There were no reductions in the EBV titers. The patient was continued on oral azidothymidine.

THP.236 Phase I study of the use of Lymphoblastoid interferon HuIFNα(Ly) and Difluormethyl-ornithine (DFMO) in the treatment of Acquired Immune Deficiency Syndrome (AIDS) related Kaposi's sarcoma.

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HuIFNα(Ly) is active against AIDS-related Kaposi's sarcoma. (JCO, 1985:506). DFMO augments the in vitro antitumor activity of interferon. In addition, DFMO may be protective against the development of Pneumocystis carinii pneumonitis. We therefore are conducting a phase I study aimed at defining the maximum tolerated dose (MTD) of the combination of HuIFNα(Ly) and DFMO in patients with AIDS-related K.S. The treatment plan consists of the administration of HuIFNα(Ly) at a dose of $20x10^6$ units/m^2 intramuscularly (IM) daily x 30 days followed by the administration of HuIFNα(Ly) and DFMO in combination. The dose of HuIFNα(Ly) remains the same and DFMO was initiated at a dose of 6 grams/m^2 by continuous infusion every day x 60 days.

Nine patients with AIDS-KS have been treated and major toxicities have been thrombocytopenia and proteinuria. One patient has had a partial remission.

It is anticipated that $20x10^6$ units IM daily x 21 days every 28 days (8 days of rest period) with daily continuous intravenous administration of DFMO at a dose of 3 grams/m^2 will be the MTD for this combination. Phase II studies will then be conducted to determine the therapeutic efficacy of this combination in the treatment of AIDS-related K.S.

THP.237 Treatment of cytomegalovirus pneumonitis with foscarnet (trisodium phosphonoformate) in patients with AIDS

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Cytomegalovirus (CMV) is a frequent opportunistic infection in patients with AIDS and is associated with both high morbidity and mortality. CMV pneumonia has proved particularly difficult to treat with other experimental agents including 9-(1-3-Dihydroxy-2-propoxymethyl) guanine (DHPG). Foscarnet (trisodium phosphonoformate) has shown probable benefits when used for serious CMV infections in other immunosuppressed patients and we therefore undertook an initial study of this agent in AIDS patients with CMV pneumonia.

Eight patients were included. Diagnosis of CMV pneumonia was based on the typical clinical features together with viral culture and the detection of early antigen fluorescent foci (DEAFF) with monoclonal antibodies in bronchoalveolar lavage specimens obtained prior to treatment. Following an initial bolus of 20mg/kg, foscarnet was administered as a continuous intravenous infusion via a peripheral vein for between 8 and 26 days. The infusion aimed at keeping the plasma foscarnet level at 150µg/ml. Four patients had co-existing pneumocystis carinii (PCP) which had been treated for at least 3 days without clinical improvement prior to foscarnet therapy. Therapy for PCP was continued in all patients. All 8 patients improved following treatment, and 7 left hospital.

Side effects included minor thrombophlebitis, reversible rises in serum creatinine and reversible anaemia. These results suggest clinical benefit of foscarnet in CMV pneumonia and a controlled trial is being undertaken.

THP.238 Foscarnet-treatment in HIV-infected homosexual men.

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Phosphonoformic acid (Foscarnet) is an antiviral agent with in vitro activity against some retroviruses including HIV, all human herpes viruses and Hepatit B virus. Foscarnet selectively inhibits DNA-polymerases and reverse transcriptases. April -85 - April -86 14 men aged 20-42 with PGL or ARC and positive HIV-cultures were treated with continuous infusion of Foscarnet solution in periferal veins. Treatment period was 2-3 weeks with a dosage of 0.14-0.16 mg/kg/min. Pharmacokinetics and clinical effects were studied.

Results: Side effects. In 4 pats treatment was discontinued due to nausea. Nausea, headache and fatigue were most frequent and correlated to Foscarnet plasma levels. All pats had a slight to moderate rise in their Se-Krea. levels. All side effects were rapidly reversible.

Clinical symptoms such as nights sweats, bowel disturbances, fever periods temporarily disappeared or improved in about 80 %. The placebo effect must however be regarded as high. Follow up period was 3 - 4 months.

Viral isolations. HIV was isolated in 20/25 cultures taken 6 months - 2 days before treatment and in 14/39 cultures from the last day of treatment - 4 months after. T_4 and T_8 cells and immunoglobulins remained unchanged. Lymphocyte stimulation tests showed no significant changes.

Conclusions: In view of Foscarnets broad antiviral spectrum, the encouraging clinical and virological results of this study and the reversibility of side-effects, further and controlled studies are important. Intermittent administration of Foscarnet for longer periods but with lower doses may be one way. In vivo antiviral effect against HIV remains to be proven for Foscarnet as well as for other antiviral drugs against HIV.

THP.239 *Immunological and clinical response to Cyclosporin in 25 HIV seropositive patients.*

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Cyclosporin 7.5 mg/kg daily was given to 25 HIV seropositive non-AIDS patients. Their characteristics were: mean age: 36 years (range 20-56), sex: males 21, females 4, stages II (T4 cells/ul > 300, < 600): 15, stages III (T4/ul <300): 10. 8 were asymptomatic, 14 had persistant generalized lymphadenopathies and 3 had constitutional symptoms.The drug was given for 3-6 months with the hypothesis that it could inhibit both HIV replication and the potential auto-immune component of HIV disease. A sustained and significant increase over 600 T4/ul occurred in 7 stages II and 1 stage III. A transient T4 cell peak was only observed in the other patients. T8 cells/ul which were > 800 in 16 cases sharply decreased in 11 patients and lymphadenopathies disappeared in 14/16. After cyclosporin withdrawal T4 and T8 cells as well as lymphadenopathies returned to pre-treatment status within 2 months. The evolution of treated patients was compared to that of a matched control group of 56 subjects. After a mean follow-up of 11 months, 9/14 control and 3/10 treated stages III evolved towards AIDS (2 oesophageal candidiasis, 1 reversible Kaposi's sarcoma) ; the figures were 4/42 and 0/15 for stages II. Cyclosporin side effects (hypertension, creatinine increase and anaemia) were moderate and reversible. These results might stimulate biological research as well as clinical trials with Cyclosporin in selected groups of HIV seropositive subjects with the aim of delaying or preventing AIDS occurrence. Updated results will be presented at the time of the Conference.

THP.240 Immune Parameters of Patients with Acquired Immune Deficiency Syndrome (AIDS) /Kaposi's Sarcoma (KS) during Human Lymphoblastoid Interferon Treatment

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Immune parameters were assessed for 35 patients with AIDS/KS before and longitudinally during treatment with human lymphoblastoid interferon (IFN) (Wellferon). IFN was given intramuscularly at a dose of 20mg/m^2 daily for 8 weeks, and patients without progressive disease continued receiving interferon 3 times per week. Immunologic parameters assessed included mononuclear cell surface marker analysis; natural killer cell activity (%CYT) determined on an effector cell (CD16+):target cell (K562) ratio of 1:1; proliferative responses to mitogens and antigen; and serum immunoglobulin levels. Upon enrollment to therapy protocol, patients had significantly decreased leukocytes, numbers of lymphocytes, %CD4+ cells; increased %CD8+ cells, %CD16+ cells and %CD14+ cells; decreased %CYT; decreased proliferation to mitogen and antigen stimulation; increased IgG and IgA compared to normal values. After 12 weeks of therapy, the patients remaining on protocol showed significant decrease in leukocyte count, in lymphocyte count, and in proliferative responses to phytohemagglutinin. There was a significant increase in %CD4+ cells and increase in %CYT to K562 cell line (p=.05 repeated measures analysis of variance). A second group of 22 AIDS patients with more extensive KS received vinblastine administered intravenously at a dose of 5mg/m^2 every 2 weeks concurrently with IFN therapy. These patients did not show increase in %CD4+ cells or increase in %CYT after 12 weeks on therapy. These data suggest some degree of immunomodulation in these patients as a result of in vivo INF therapy which was not seen in patients with more extensive disease who recived INF plus chemotherapy.

THP.241 Clinical and Immunologic Improvement in AIDS/ARC Patients Treated with IMREG®-1, an Immunosupportive Agent

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IMREG®-1, a potent immunosupportive agent, isolated from normal human leukocytes by a series of HPLC separations, contains an active small peptide whose composition indicates that it may be an important link between the neuro-endocrine and immune systems. IMREG®-1 augments delayed hypersensitivity (DTH) to recall antigens, and enhances the production of MIF, LIF and IL-2 by stimulated T4+ helper cells.

50 patients with AIDS/ARC have been repeatedly treated with IMREG®-1 in protocols lasting several months. Such treatment results in return of DTH in anergic patients, which is associated with enhanced mitogen induced proliferative responses and IL-2 production. Such responses have been noted in over 60% of patients, and are associated with sustained stabilization of hematocrit, platelet and total lymphocyte counts. T4+ helper cell numbers increased or did not fall in 23 of 48 patients who were followed for three months. Weight gain, clearing of refractory oral candida and a decline in serum hyperglobulinemia and uric acid levels were noted in some patients. IMREG®-1 has a peak action at 7 to 10 days. The most beneficial results were observed in patients having a minimum residual of 100 T4+ cells/mm^3. There has been no observable toxicity following prolonged administration of IMREG®-1 for up to three years.

The ability of IMREG®-1 to reconstitute the ability of AIDS/ARC patients to mount antigen-specific immune responses is a fundamental indication of the effect of this agent on HIV-induced immunodeficiency. These important effects on the immune system coupled with the beneficial clinical effects observed suggest that IMREG®-1 appears to be useful in ameliorating the immunodeficiency seen in AIDS/ARC patients.

THP.242 Variable Serologic Status in Children with Hypogammaglobulinemia (HG) and Transfusion (TX) Induced HIV Disease

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As part of a prospective study of highly transfused infants and children, we have identified two children with EIA positive, Western blot (WB) confirmed HIV disease and subsequently identified HIV infected donors in both. Both children had profound HG at the time of receipt of the implicated tx and for a time subsequent to its receipt. They had received units of fresh frozen plasma (FFP) from different donors at 2 days of age for treatment of severe hyaline membrane disease and at 5 years of age during therapeutic plasmapheresis for immune thrombocytopenia, from which both recovered. Both patients remain EIA/WB positive; one has oxygen dependent bronchopulmonary dysplasia, is now normoglobulinemic, with normal T4/T8 ratio and has positive HIV cultures, now 2 1/2 years post receipt of the FFP. The other has biopsy proven lymphoid interstitial pneumonitis, has normal immunoglobulins but reversed T4/T8 ratio. Two additional children were identified as recipients of blood from HIV infected donors but were EIA, RIP and WB negative repeatedly despite clinical presentation and symptoms of AIDS/ARC in both. One received washed packed red blood cells (PRBC) at 25 days of age and the other FFP at 34 days of age. Both were 26 week gestation premature infants who had multiple episodes of fungal & bacterial sepsis, pneumocystis pneumonia, monoliasis and thrombocytopenia culminating in death at age 49 months and 10 months, respectively. One had normal immunoglobulins for age prior to receipt of the implicated unit. Both developed profound HG. One of the two was cultured for HIV and had positive reverse transcriptase activity on day 21 of culture. Autopsies on both were consistent with HIV disease. These data suggest that post-transfusion HIV infections result in variable serological manifestations and that EIA/WB tests alone may be inadequate diagnostic tools to document HIV disease in some children with HG.

THP.243 EVALUATION OF A SYNTHETIC PEPTIDE BASED HIV-EIA. Barbara Hosein, William Ying, Louis Baker, William R. Oleszko, Beverley Lightbourne, and Celso Bianco. The New York Blood Center, NY, NY.

Our center has evaluated a synthetic peptide based ELISA assay for antibody to HIV developed by UBI-Olympus. The solid-phase antigenic adsorbent employs polypeptides synthesized chemically with sequences corresponding to highly antigenic segments of both envelope (gp41) (PNAS 83, 6159-63, 1986) and core (P24) proteins of HIV.

The initial reactive rate in 2000 random donors who designated their units for transfusion is 0.85% and the repeat reactive rate is 0.25%. Of the repeat reactive samples, 40% are positive by Western Blot (WB) analysis. The specificity if this assay is 99.85%.

Samples (n=505) found to be repeat reactive in other licensed HIV antibody assays at our center were retested with the synthetic peptide-based assay. All of the 419 WB positive samples tested were reactive, whereas only 2 of the 86 WB negative samples were reactive.

Sequential samples (n=90) collected at short intervals from 13 individuals who seroconverted during the period were tested by this assay, by those of six other manufacturers, and by WB. The peptide based assay detected HIV antibodies earlier than did all other ELISAs in 2 individuals and earlier than or equal to all other ELISAs in ten other individuals. It detected HIV antibody two to five weeks prior to detection by WB in 5 of the 13 individuals.

The synthetic peptide based assay has the potential to eliminate non-specificity associated with host cell antigens. Its detection of antibody in all WB positive samples studied and its high sensitivity in seroconversion samples suggest that all individuals exposed to HIV make antibodies against a restricted set of amino acid sequences of HIV.

THP.244 IMPAIRED CELL MEDIATED IMMUNITY (CMI)IN HAEMOPILIA

R MADHOK JA GRACIE E FOLLETT A BURNETT GDO LOWE CD FORBES GLASGOW ROYAL INF UNI DEPT MED GLASGOW SCOTLAND

We and subsequently others have shown that lyophilised factor concentrates are in immunosupressive in vitro.The aim of this study was to determine if haemophiliacs treated with factor concentrate show immunosupression.The CMI response was evaluated in 29 haemophiliacs by means of the DNCB skin test.All patients had a response below the lower limit of the normal range.No difference was seen in the skin response between pts positive and negative for HIV In the whole grp.&in seronegative pts.(N=17)there was an inverse correlation between clotting factor concentrate exposure &the skin response .In HIV positive pts no such association was apparent.

The T-4 count showed a correlation (r=.49)with the skin response in HIV negative patients but not in HIV positive pts.In positive pts.a correlation was seen with T-8 cnt.(r=.45).

This study shows that clotting factor concentrate impairs the CMI response to a new antigen in the absence of HIV infection .Future studies may show a lower response in positive patients as HIV immunosupression may take years to devlop.

THP.245 Characterization of HTLV-III (HIV) and HTLV-I Antibody Reactive Sera by Specific Western Blot Assays. STEVE S. ALEXANDER, A.J. BODNER, A.J. CORRIGAN, T. CLEMENT AND W.R. FREDERICK*, Biotech Research Laboratories, Inc., Rockville, MD and *Howard University Cancer Center, Washington, D.C.

Western Blot assays have been developed to identify the antibody specificity of HTLV-III (HIV) and HTLV-I ELISA reactive samples. Most strongly reactive HTLV-III samples contain antibodies to all major viral proteins: ENV (gp41/160), GAG (p17, p24/55) and POL (p31, p51/66). HTLV-I reactivity is primarily directed against the major gag proteins p19, p24 and their intermediates.

Both Western Blot assays were carried out on a large group of predominantly black IV drug users. More than half of the positive sera were reactive in both assays. The majority of these samples contained antibodies to the major viral proteins of both viruses indicating co-reactivity rather than cross reactivity. Previous analysis of another group of HIV positive on HTLV-I and a HTLV-I group on HIV demonstrated minimal cross reactivity. Concomitant infection with HTLV-I and HIV has been reported (Harper et al. (1986) New Eng. J. Med. 315, 1073-1078). Our results indicate a significantly high frequency of dual exposure/infection among this particular at-risk population.

THP.246 Assessment of the Demographic and Motivational Characteristics of HIV Seropositive Blood Donors

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Seventy five male and 14 female blood donors found to be confirmably HIV seropositive during routine blood donor screening, together with age and sex matched controls, have been enrolled into a five year multi-center prospective study. For 59 males (78%), the primary hierarchical risk for HIV infection was sexual contact with other males; the mean number of partners was 25.5 (range 1-250). Of 14 males whose primary risk was parenteral, 8 had a history of IV drug use, and 6 had a history of prior transfusion. No established AIDS risk factors were found during interviews with 8 seropositive males. Of the 14 HIV+ females enrolled, the primary hierarchical risk of HIV exposure was sexual contact with bisexual or IV drug abusing males (50%). Parenteral exposure via drug use or transfusion was the primary risk for 4 seropositive females. No AIDS risk factors could be determined for 5 females. Prior STDs were reported in 52% of index donors vs. 9% of controls.

Forty five percent of index donors suspected that they were in an AIDS risk group at the time of donation. These individuals reported the following motivations for blood donation despite self-deferral measures: peer pressure to proceed with donation (29%), desire to learn HIV status (29%), self-denial of risk status, or impression that their blood was of particular value (61%), appeal for self-deferral not taken seriously (6%). Additional interview data indicated that 65% of donations from subjects with self-recognized AIDS risk would not have been excluded by a confidential designation that their blood donation should not be used for transfusion.

THP.247 Comparative HIV Antibody Testing in Blood Donors

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We have screened 164,775 blood donations for antibody to HIV by two ELISA's: 120,229 samples were tested by Abbott EIA from Mar. '85 - June '86; 44,546 samples were screened by the DuPont ELISA from July '86 - Dec. '86. The Abbott initial reactive rate (IR) ranged from 0.2 - 5.8% per week; the repeat reactive rate (RR) was .44% (range: 0 - 1.5%). Abbott Western blots (WB) on 531 RR samples were: 488 (.41%) negative, 12 (.01%) positive and 31 (.03%) atypical. The DuPont IR rate was .4 - 1.1%; the RR rate was .57% (range .2 -.8%). WB performed at Biotech Research Labs (BTRL) on 255 repeat reactive samples were: 114 (.26%) negative, 3 (.007%) positive and 138 (.31%) atypical. Samples found to be WB positive or atypical were submitted to both labs for comparison. The same 15 samples were identified as WB(+) by both labs but there was a wide variation in the reporting of atypical WB. Of the 31 samples originally reported as Abbott WB atypical, 27 (87%) were DuPont ELISA (-) BTRL WB (-). Subsequent samples on 17/31 have remained DuPont ELISA(-) BTRL WB(-), 4 others remain BTRL WB atypical. Of the 138 BTRL WB atypical samples, 128 (93%) were Abbott WB(-) and 10 (7%) were atypical. Eleven of the Abbott (-) DuPont (+) BTRL WB atypical donors have returned for subsequent donations. Seven of 11 remain BTRL WB atypical, Abbott EIA(-) WB(-); 2/11 are now negative on all assays. Two remaining Abbott EIA(-) DuPont ELISA(+) donors with p24 on both WB's, returned within 2 months, were reactive on both screening assays and were fully positive on both WB. The original samples from these donors are reactive on the recently licensed modification of the Abbott EIA. These results suggest that sensitivity and specificity of screening tests are evolving and that there is considerable variation in WB procedures. Ongoing comparative testing of blood donors is essential to assess assay performance and develop donor notification strategies.

THP.248 HIV Seroconversions after Heated Clotting Factor Concentrates in Hemophiliacs.

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In Italy, heated concentrates became the only source of hemophilia therapy since July 1985. Since then 63 anti-HIV seronegative hemophiliacs treated with heated concentrates were followed-up prospectively, focusing on seroconversions. Anti-HIV (documented by ELISA and WB) occurred in 6 patients without other risk factors for HIV infection. For 3, anti-HIV was first found in Sept., Oct. or Nov. 1985. Another patient seroconverted in Sept. 1986, but no sample was available after the last negative test (Nov. 1985). For these 4 cases we cannot exclude that seroconversions are due to nonheated concentrates. The remaining 2 patients seroconverted in July 1986. For both, a hemophilia A patient (treated only with a concentrate dry-heated for 72 hr at 68°C) and a hemophilia B patient (treated with both a steam-heated and a dry-heated concentrate for 72 hr at 68°C) the last seronegativities were found in March 1986, i.e. 7.0 and 7.5 months after commencing the use of heated concentrates or 3.5 and 4.0 months before the first seropositivity. In conclusion, two seroconversions occurred in previously seronegative patients treated exclusively with heated concentrates. Intensity and duration of concentrate exposure to heating were greater than those for dry-heated concentrates (60°C for 30 hr) that induced two reported seroconversions.

THP.249 Experience with a Competitive ELISA for HIV Antibody in Blood Donors in the USA

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Sera and plasma from 12150 blood donors at 4 different geographic locations were tested with a competitive ELISA for anti-HIV antibody (Wellcozyme, Wellcome Diagnostics; Dartford, England). Samples were tested in parallel at each site with a noncompetitive assay for HIV antibody. All samples initially reactive by either HIV ELISA were retested by Wellcome and examined by western blot. The Wellcome ELISA results obtained by the 4 laboratories are given below:

		INITIAL REACTIVES		REPEAT REACTIVES	
Laboratory	# Samples Tested	No.	%	No.	%
A	3,137	6	0.19	2	0.06
B	3,018	7	0.23	1	0.03
C	3,001	6	0.20	1	0.03
D	2,994	1	0.03	0	0
TOTALS	12,150	20	0.16	4	0.03

Only 1 of the 65 initially reactive specimens was reactive on repeat test in both HIV assays. This sample was also reactive by western blot.

THP.250

ABSTRACT NOT AVAILABLE AT TIME OF PRINTING

Epidemiology—HIV-AIDS Cofactors

F.1.1 U.S. Department of Defense HIV Testing Programs: An Overview.
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In 1985 and 1986 the US Department of Defense instituted programs for routine HIV testing of the following populations: civilian applicants for military service, active duty personnel, National Guard, and Reserves. Separate programs are conducted by the Army, the Air Force, and the Navy and Marines. In all programs, sera are screened by ELISA, and repeatably positive specimens are tested by Western blot. Through December 1986 over 1.9 million persons have been tested. The mean prevalence rate of positive Western blots among civilian applicants for military service is 1.5 per 1000 and among active duty personnel it is 1.6 per 1000. Age, male gender, and black racial group are independent risk factors for seropositivity. The ratio of male:female prevalence rates is 2.5:1. A summary of prevalence data and of demographic factors associated with HIV seropositivity is presented.

F.1.2 HLA Phenotypes are Possible Risk Factors for Development of AIDS.
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To evaluate a possible immunogenetic role for developing AIDS, we HLA typed 226 white homosexual males, 91 who were HIV seronegative, 135 seropositive of whom 56 had AIDS (28-Kaposi's (KS), 28-opportunistic infections (OI)or subsequently developed AIDS. The frequency of individual HLA antigens in the HIV negative population was similar to North American caucasians. HLA-DQ1 was higher in frequency in all AIDS patients (77%) compared to HIV^+ non-AIDS individuals (56%). HLA-DR1 was higher in frequency in OI patients (39%) compared to KS (25%) and HIV non-AIDS (16%) HLA-DR3 frequency was 36% in OI patients, 14% in KS and 28% of the at risk group. HLA-DR7 was found in 29% of KS compared to 4% in OI (HIV^+ non-AIDS, 19%). HLA-DRw53 was also higher in frequency in KS (60%) compared to OI (15%) (HIV^+ non-AIDS, 44%). In 106 HIV^+ individuals enrolled in the study in 1982, 44%±14% DR1 individuals developed AIDS during this 4 year period while AIDS occurred in only 19%±5% DR1 neg. individuals. Total numbers of $CD4^+$, $CD8^+$ cells were virtually identical in 1982. These data demonstrate that the HLA-DR phenotype may be associated with an increased risk for developing AIDS after exposure to HIV and that certain phenotypes may be associated with KS or OI. The mechanism whereby this risk is conferred is not demonstrable. However since HLA-D region molecules are recognition elements in the immune response, specific molecules may tend to promote or protect in development of AIDS.

F.1.3 Familial Tendency to Serious Sequelae of HIV Infection.
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Cofactors for the development of serious complications of HIV infection are not well recognized. To ascertain if genetic factors might contribute to the outcome of HIV infection, we examined 34 sibships wherein at least two siblings with classic hemophilia had serologic and/or clinical evidence of HIV infection.

HIV-infected subjects were classified as having a) no symptoms (with or without generalized lymph node enlargement) b) AIDS related complex (ARC), c) AIDS, d) thrombocytopenia (T) (<150,000 platelets/uL on at least 2 occasions) e) leukopenia (L) (<3,000 WBC/uL) or combinations of clinical and hematologic manifestations.

As of December 1986, 31 of 52 patients for whom complete information was available were asymptomatic. 5 of 52 had developed ARC. 5 of 52 had developed AIDS. 8 of 68 had L. 13 of 68 had T. Siblings of patients with AIDS or ARC had a 75% chance of having AIDS, ARC, L or T as opposed to an 11% risk of these complications among sibs of asymptomatic hemophiliacs ($p = 0.003$, Fisher Exact). The risk of AIDS or ARC among sibs of patients with AIDS or ARC was 33% vs. a 10% risk among sibs of patients without AIDS or ARC ($p = 0.22$) Siblings of patients with T or L had a 44% chance of also having T or L as opposed to a 12% chance among sibs of patients without T or L. This concordance was almost significant ($p = 0.06$). These data suggest that there is a familial tendency to certain serious complications of HIV infection or that other factors common to sibs may contribute to the outcome of HIV infection. These observations warrant longitudinal follow-up of sib pairs and expansion of the study to identify factors that affect the outcome of HIV infection.

F.1.4 Age and Cumulative Incidence of AIDS among Seropositive Homosexual Men in High Incidence Areas of San Francisco.
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From a probability sample of homosexual men living in 19 census tracts of San Francisco where AIDS was most prevalent, we estimated the age-specific prevalence of infection by HIV. By March 31, 1986, 805 cases of AIDS were diagnosed among an estimated 8,346 seropositive men, aged 25-54, in this area, yielding a rate of 96.5 cases per 1,000 seropositives (95% confidence interval, 86.6 to 108.8 per 1,000). Cumulative incidence was more than twice as high among older (aged 35-54) than among younger (aged 25-34) men (144.5 vs. 67.8 per 1,000, $p<.001$).

To investigate whether or not the association between age and cumulative incidence was due to earlier infection of older men, we examined the relation between current age and serostatus in 1978 in a sample of 394 homosexual men from the San Francisco City Clinic Cohort. There was no relation between age and early infection in this sample. Moreover, age was inversely related to the rate of seroconversion from 1978 to 1984 (chi-square test for trend = 11.4, 1df, $p<.0001$).

We conclude that the higher cumulative incidence of AIDS among older men cannot be explained by the hypothesis that older infected men seroconverted earlier than younger infected men. Other hypotheses, including the possible effects of age-related co-factors of disease progression and of biological aging, need to be examined.

F.1.5 Hepatitis B virus coinfection in homosexual men seropositive for human immunodeficiency virus antibody
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Among subjects positive for anti-HIV in a cohort of initially healthy homosexual men under prospective study for risk of AIDS, we examined the association of HBsAg with impairment of cellular immunity and progression to AIDS. At baseline 62% (292/469) were seropositive for anti-HIV and 87% (410/469) had one or more serological markers for HBV. Of HBV seropositives, 10% (39/410) were seropositive for HBsAg and of HBsAg seropositives 74% (29/39) were also positive for anti-HIV. Among the 29 HBsAg carriers who are anti-HIV positive, 1 developed AIDS (3%) over 2 years of followup compared to 40 of 258 (16%) anti-HIV positives who are not HBsAg carriers (OR=0.19,p=0.057). Comparing anti-HIV positive subjects with any HBV antibody marker with subjects with no HBV marker, 38 of 240 (16%) HBV Ab positives developed AIDS versus 2 of 15 (13%) without HBV markers (p=0.78). Among anti-HIV seropositives, HBsAg carriers were significantly less likely at baseline to have an H/S ratio below 0.6 (OR=0.29, p=0.025). At 1-year followup HBsAg carriers were again less likely to have an H/S ratio below 0.6 (OR=0.31,p=0.08). These observations suggest coinfection with HBsAg may be associated with reduced pathology of HIV infection.

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F.1.6 Association of Anogenital Ulcer Disease with Human Immunodeficiency Virus Infection in Homosexual Men
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To test the hypothesis that genital or anorectal ulcer disease predisposes to acquisition of HIV, 2 groups of homosexual men (HM) were studied. Type-specific herpes simplex virus (HSV) antibody (Ab) was measured by Western blot (WB); HIV Ab was analyzed by ELISA (Genetic Systems) and WB; the hemagglutination treponemal test for syphilis (HATTS) was performed. Of 176 HM with acute proctitis or enteritis, all of whom participated in receptive anal intercourse, 103 (59%) had HIV Ab and 145/167 (87%) had Ab to HSV-1 and/or HSV-2. HSV-2 Ab was present in 77% of subjects with HIV Ab, compared with 37% of those without HIV Ab (P<0.0001). By logistic regression, controlling for numbers of sex partners in the preceding 1 mo, 6 mo and lifetime and years of sexual activity, the following were significantly associated with HIV Ab: HSV-2 Ab (odds ratio [OR]) 4.0, P=0.0005), past history of genital or anorectal herpes (OR 2.7, P=0.018)), past oral herpes (OR 4.0, P=0.02), and past syphilis (OR 4.8, P=0.0007). In a separate group of 109 HM seeking AIDS counseling, HSV WB was performed in 99; HSV-2 Ab was present in 31 (74%) of 42 HIV-positive and 15 (26%) of 57 HIV-negative subjects (P<0.0001). HATTS was reactive in 9 (18%) of 49 HIV-positive and 3 (5%) of 60 HIV-negative subjects (P=0.047). These associations also persisted when controlling for number of sex partners. Past HSV infections and syphilis are significant risk factors for HIV infection in HM, perhaps because they cause mucocutaneous ulcers that facilitate HIV acquisition.

Virology—Diagnostics

F.2.1 Correlation between Antibody Response to HIV Antigens, Neutralizing Antibody Titers and Clinical Status.

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The antigen specific antibody response in 159 sera from HIV seropositive patients has been analysed by Western blot. The samples were including two sequentiel sera from two groups of individuals. Group 1 was corresponding to individuals with no evolution in the disease (5 asymptomatic carriers, 28 lymphadenopathy and 4 ARC patients). Group 2 was corresponding to patients who developed AIDS (3 asymptomatic carriers, 15 lymphadenopathy and 6 ARC patients) In the first group, the mean time between the 2 serum samples was about 30 months whereas in the second group, the mean was approximatively 17 months and the second serum sample was at the time of the disease. A lower antibody response to viral antigens was observed mainly in group 2. Neutralizing antibody activity of 18 sera from group 1 and of 22 sera from group 2 was also studied. In group 1, 4 out of 9 patients presenting high antigen antibody response have increasing neutralizing titers with no changes in Western Blot patterns. In group 2, 9 out of 11 patients have constant or decreased neutralizing titers and antibody response. The decrease of neutralizing antibody titers seems to correlate with the lower antibody response observed in the second serum sample. The lower reactivity of this sample by Western Blot was concerning mainly the one to HIV core antigens. Such prospective studies might be important for predictive status of the disease outcome.

F.2.2 Virologic Studies in the Diagnosis of Pediatric AIDS

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The diagnosis of AIDS virus infection in infants during the first 12 months postpertum is complicated by the presence of maternal anti-viral antibody. Virus isolation in infants who present with or subsequently develop AIDS-essociated clinicel diseese was positive in 78/94 (83%) cases on the first isolation attempt. All virus positive infants were seropositive in immunoessays with virion p24 and bacterially synthesized components of gp41 protein. Two approaches have been utilized to provide surrogate tests for virus isolation which is currently the definitive leboratory measure of infection. First, decline of maternal antibody was evaluated in 6 infants who were born to seropositive mothers but were themselves not infected as evidenced by normal clinical, immunologic and virologic findings in a follow-up everaging 36 months (range 26-50 months). Both p24 antibody and gp41E antibody declined to baseline by 12 months from high levels immedietely post-partum. Conversely, by 12 months of age, all infected infants had easily detected antiviral antibodies. The second approach was to utilize a p24 antigen detection ELISA on serum and plasma from virus positive infants. Antigen positive plasma from 18 infants was virus positive in 17 instances; 15 patients were antigen negative but virus positive; all antigen negative virus positive patients had high levels of anti-p24 antibody. No antigen negetive, antibody negative, virus-positive infants have been detected in over 125 infants that have been tested. Thus, it is possible to utilize a combination of p24 antigen detection and anti-p24 antibody determination in pediatric patients to achieve objective laboratory diagnosis of AIDS virus infection.

F.2.3 Identification of HIV Sequence in DNA Extracted Directly from Peripheral Blood Lymphocytes and Bone Marrow Using In Vitro DNA Amplification.

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While serological tests have significant sensitivity and specificity for the identification of antibodies against HIV, they do not provide direct identification of the virus. The identification of virus generally requires co-cultivation of patient specimen with permissive cells, followed by either assays for reverse transcriptase activity, immunofluorescence using antibodies to the structural components of the virus, or Southern blot analysis. Because the number of infected cells is generally low and due to transcriptional domancy, these procedures are often inadequate for detection of virus.

We have used the polymerase chain reaction (PCR) and oligomer restriction (OR) procedures to amplify and detect HIV viral sequences. These procedures are both sensitive and specific for HIV and can detect as few as 25 genome copies in 200,000 cells. Previously, we reported the successful identification of HIV sequences in cell lines established from AIDS and ARC patients. These included cell lines that were devoid of reverse transcriptase activity and/or negative by Southern blot analysis. We report here that PCR-OR can identify HIV viral sequences in DNA extracted from mononuclear cells of fresh blood and bone marrow, thereby eliminating the lengthy process required for cell culturing. Notably, these procedures have also made possible the identification of HIV viral sequences in asymptomatic, seropositive individuals as well as in seronegative, culture positive individuals who are at risk for AIDS. Optimization of the amplification procedure and overall sensitivity and specificity of the assay will be presented.

F.2.4 Double HIV-1 and HIV-2 seropositivity in four patients in Paris.

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The presence of antibodies to both HIV-1 and HIV-2 has already been described in sera from AIDS patients in Central African Republic and Ivory Coast. This double seropositivity is probably not a recombinent event but rather a double infection. We report here four cases of double HIV-1/HIV-2 seropositivity in patients (pts) who have been living in France for several years. Two originated from West Africa: pt1 (21 years) born in Ivory Coast has been living in France since 1984, he is a heterosexual single male with numerous partners, one beeing an intravenous drug abuser. Pt2 is a 37 years old female from Ghana, having had 2 Ghanaian partners and living in France since 1978. Pt3 (37 years) and 4 (33 years) are white homosexual males, pt3 having multiple West African partners since 1980. All the 4 pts presented with AIDS-related complex (group III, subgroup A) diagnosed in 1986.

In the 4 pts IgG antibodies to HIV-1 and HIV-2 were detected by Elisa and Western blot (Diagnostics Pasteur). Double HIV-1/HIV-2 seropositivity was demonstrated on the presence of antibodies to HIV-1 (gp160-gp110 and gp41) and HIV-2 (gp130-gp105 and gp 41) envelope glycoproteins. In pts 2, 3 and 4 immunoblot analysis showed variable reactivities against the gag and pol gene products of HIV-1 and HIV-2. A similar banding pattern for HIV-1 and HIV-2 was observed in sera collected in 1985 for pt3 and in 1984 for pt4. Retroviral isolates were performed from the peripheral blood lymphocytes of the 4 pts. Isolates were caracterized by Southern blot analysis. Neutralizing antibodies to HIV-1 and HIV-2 were evaluated.

These data showed that HIV-2 infection was present in the french gay community in 1984. To diagnose HIV-1/HIV-2 double infection HIV-1 and/or HIV-2 Elisa positive sera should be checked by HIV-1 and HIV-2 Western blot. Evaluation of the pathogenicity and the extent of this double HIV-1/HIV-2 infection is needed.

F.2.5 Efficacy of five HIV enzyme immunoassays (EIA) in detecting antibody to HTLV-IV.

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Recent seroepidemiological studies show that STLV-III related human retroviruses (HTLV-IV, LAV-II) are widely present in West-Africa. Moreover HTLV-IV- or LAV-II- seropositive subjects have been found occasionally in Europe. Since no type specific ELISA is yet available we have compared the performance of 5 HIV commercial EIAs in detecting cross-reactive antibodies to HTLV-IV. The assays evaluated were from Abbott, Organon, Pasteur (two wells) and Wellcome. A fifth EIA, from Abbott, was also evaluated. This EIA is a competitive immunoassay employing as antigen recombinant DNA-produced HIV proteins (ENVACORE®). In this assay every sample is tested for the presence of antibody to either core proteins or envelope proteins. Preliminary results on 26 sera from healthy West-African residents positive for antibody to HTLV-IV (serotype specificity assessed by western-blot and/or radioimmunoprecipitation) indicate that the HIV test kits are not equally efficient in detecting HTLV-IV antibody positive sera. The Wellcome test was the less sensitive (42 % positivity) whereas the ENVACORE® kit was the more sensitive (96 % positivity). The Organon, Pasteur, and Abbot first generation EIA kits detected 73 %, 81 %, and 92 % of HTLV-IV antibody positive sera, respectively. Futhermore, approximately 50 % of people exposed to HTLV-IV develop antibodies that cross-react with a recombinant DNA derived HIV antigen from the env region containing all amino acids of gp 41 as well as a portion of gp 120. These results indicate that the env gene products of HIV and HTLV-IV are conserved to the degree that they are serologically cross-reactive. Results on larger series will be presented.

This data must be considered when regarding African seroepidemiological studies as well as screening of blood donors.

F.2.6 Diagnosis of HIV Infection: Utility of Radioimmunoassays for the Major Internal Antigen (p24) and Transmembrane Envelope Glycoprotein (gp41) of Human T-Cell Lymphotropic Virus, Type III (HTLV III).

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The radioimmunologic techniques have provided invaluable avenues in epidemiologic studies of retroviruses. In the present studies we have developed specific and sensitive immunoassays for the major internal antigen (p24) and the transmembrane envelope glycoprotein (gp41) of HTLV III purified from the density gradient banded virus preparations. In an attempt to evaluate their utility in diagnosis, sera from patients with acquired immunodeficiency syndrome (AIDS), AIDS related complex (ARC), clinically asymptomatic as well as normal individuals were tested for antibodies to p24 and gp41. High titered antibodies to gp41 could be readily detected in 100% of the sera from AIDS patients, whereas, only 70% of these patients exhibited antibodies to p24. These data, along with the analysis of sera obtained from sequential bleeds of patients throughout the course of infection and the disease, indicated that antibodies to gp41 persist, while the antibodies to p24 are either not detected or have much lower titers during late stages of infection. The sera from the individuals which lacked detectable levels of antibodies to p24 were subjected to an enzyme linked immunoassay which detects presence of HIV antigens (predominantly p24) in the body fluids. These analyses revealed that in a large number of cases, the lack of antibodies to p24 in the sera correlated with the presence of HIV antigen. Based on these observations, the antibodies to gp41 are the most consistent marker for evaluation of HTLV III exposure, whereas, antibody titers to p24 may indicate various stages of the disease.

Clinical Management—Infections II

F.3.1 Cross-Allergy to Sulfonamides/Sulfones (Sulfa), and folic antagonists in AIDS

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Thirty AIDS patients who showed sulfa allergy following Pneumocystis carinii pneumonia (PCP) treatment were rechallenged with another sulfa. 21 pts received Trimethoprim-sulfamethoxazole (TS) for first episode PCP and developed a major allergy (9 rash, 10 fever, 5 ↓WBC, 1 ↑LFT's). When they received dapsone/TMP (DT) for the second PCP, 6/21 showed side effects (4 rash/fever, 1 ↓WBC, 1 ↓plates) 7-10 d after the initial dose. Four of these 21 pts also received Pyrimethamine (Pyr) and Sulfadiazine (Sdz) for toxoplasmosis; 2 showed severe rash 2 and 6 wks later. Two of 21 also received Pyr-Sulfadoxine (Fansidar) for PCP prophylaxis; 1 developed a rash after 4 wks.

Nine pts were allergic to DT for the 1st episode of PCP (7 rash/fever, 1 ↓ WBC 1 ↓ plates); all 9 received TS for 2nd episode PCP w/o side effects; 3 received Pyr/Sdz (1 developed rash at 10 days; 2 had no side effects); another received Fansidar w/o incidents. Of the 21 pts with initial TS allergy 3 were rechallenged with TS during a subsequent episode of PCP; 2 pts who received >8 d of TS developed the same side effect (rash/fever) 7 & 10 days after the initial dose. The 3rd received 4 d of TS IV w/o side effect; all finished 21 d of total therapy.

There is no cross-allergy between TS and DT; often no cross-allergy between different sulfonamides, sulfones, & folic antagonists. Rechallenge with the identical agent (TS) is often well tolerated and may be undertaken in selected circumstances.

F.3.2 Diminished Sulfa-Trimethoprim(ST) Toxicity in Blacks Treated for Pneumocystis carinii Pneumonia(PCP).

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ST therapy of PCP has been reported to produce frequent and severe toxicity in mainly white AIDS patients(pts). In 54 pts (53 blacks) with AIDS treated for PCP no ST rashes occurred. One white pt had mild rash due to oxacillin. Neutropenia(NP) was less frequent and milder and began later than reported previously despite the normally lower white blood counts(WBC) of blacks. Of 54 pts (table) 23 had NP (drop of 1000 to WBC below 2500) but only 13 had to have ST stopped (D/C). Male homosexuals (MH)(7 blacks, 1 white) had no NP. Median onset of NP was 9 days on ST. Treatment failures (ST fail), pentamidine (Pent) use and deaths paralell other reports, but toxicity is strikingly less.

GROUP	#CASES	#NP	#D/C	Onset	#ST Fail	#Pent	#Death
Females	12	6	2	14	2	3	1
Male IVDA	33	17	11	8	7	13	7
MH	8	0	0	-	5	5	1
Total**	54	23	13	9	15	22	10

(IVDA=iv drug abuser;**one MH/IVDA patient added to total)

Thirteen patients had WBC<4000 before ST therapy: 10 had slight WBC drops while on ST (mean lowest WBC=1.9; range:1.4-3.2) but only 5 required ST discontinuation. ST toxicity is markedly lower in black AIDS pts. Low WBC does not contraindicate ST as initial therapy and most blacks even with low wbc can tolerate a full ST course. Use of ST prophylaxis for PCP in blacks may be feasible.

F.3.3 Oral Therapy for Pneumocystis carinii Pneumonia (PCP) in AIDS. A Randomized Double Blind Trial of Trimethoprim Sulfamethoxazole (S) Versus Dapsone Trimethoprim (D) for First Episode Pneumocystis carinii Pneumonia in AIDS.

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Fifty-eight AIDS pts with first episode PCP and a p02 ≥60 on room air were randomized to S (TMP/SMX 20/100 mg/kg/d) or D (dapsone 100 mg + TMP 20 mg/kg/d divided by 4) for 21 days (14 days inpt; 1 wk outpt). At entry, groups were equally matched. Patients with clinical failure (severe decline by day 4 or no improvement at day 7) or severe toxicity were switched to IV pentamidine. Clinical failure occurred in 4 pts (2 S, 2 D); 2 failed at 4 days; 2 at < 24 hrs. Major toxicity occurred in 24 pts (see table); 19 additional pts had minor rash. 29 pts (34.4 %) required hospitalization for at least 4 days due to symptoms; 38 pts (65.4%) could have avoided all hospitalization. Daily monitoring for toxicity was needed in 27 (13 S, 14 D) between days 9 and 14. 55 have been followed greater than 3 months with 7 relapses in S and 4 in D.

Toxicity	S n=29	D n=29	Toxicity	S n=29	D n=29
Rash >48 hrs	2	3	Platelets <40K	1	1
WBC <750	5	1	Methemaglobin >20	-	1
LFT's 5X nl	6	1	Nausea & Vomiting	2	2

In 1st episode PCP, oral D and S are equally effective. S showed higher incidence of major toxicities (↓WBC,↑LFT's) p=.0049. Outpt therapy is appropriate for pts with p02 ≥60. Frequent laboratory monitoring is required in the 2nd week of therapy.

F.3.4 Infectious Causes of Diarrhea in Patients (pts) with AIDS.

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We retrospectively reviewed the records of 100 pts with AIDS to determine the rate and spectrum of microorganisms producing diarrhea in this syndrome. 64 pts had diarrhea documented. Diarrhea occurred in 28/35 homosexual or bisexual men (80%) compared to 37/64 heterosexual subjects (58%) (p< .05).

An infectious cause of diarrhea was found in 36/64 (56%). 11/36 (31%) were found on ova & parasite examination, 8 by stool culture, 4 by acid fast smear of stool, 4 by histological examination of a colon biopsy specimen, and 9 by any combination of these methods. Simultaneous enteric infections occurred in 9 pts. Enteric pathogens identified included Mycobacterium avium-intracellulare (MAI) in 9 pts, cytomegalovirus (6), cryptosporidium (5), salmonella sp. (5), Herpes simplex (3), candida (2), Isospora belli (2), Strongyloides stercoralis (2), and 1 each of Giardia lamblia, Schistosoma mansoni, Entamoeba histolytica, hookworm, Blastocystis hominis, Aeromonas hydrophila, Clostridium difficile, Campylobacter jejeuni, and adenovirus.

Blood cultures were positive in 19 pts. Isolates included MAI (10), salmonella sp. (5), Campylobacter jejeuni (2), and shigella (2). In 4/5 pts with salmonella and all with campylobacter or shigella, stool cultures were negative.

In 16 pts with a microorganism identified in stool, tissue, or blood, initial evaluation for the diarrhea led to the diagnosis of AIDS. In the remainder of those with infectious diarrhea, the diarrhea occurred at a mean of 7.7 months (range 1-27) after the diagnosis of AIDS.

This study demonstrates that infectious diarrhea is common in pts with AIDS. Gastrointestinal infections associated with diarrhea are often multiple (25%). MAI is the most commonly identified cause of diarrhea in our pts. Diarrhea in AIDS occurs more commonly in homosexual or bisexual men than in heterosexuals.

F.3.5 AIDS and AIDS Related Complex: Oral Manifestations and Treatment

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Fifty (50) people with AIDS/ARC, undergoing dental treatment, were evaluated for AIDS related infections and malignancies in the oral cavity. Candidiasis was the most common manifestation (53%), with the lateral borders of the tongue usually involved. Other sites were the floor of the mouth, palate, buccal mucosa and pharynx. Treatment consisted of several anti-fungal drugs, depending on severity and longevity of infection. Oral Kaposi's sarcoma lesions (32%) showed the palate and gingiva as the most common sites, while tongue and tonsillar involvement was seen. Lesions that interfere with patient comfort and function may require chemotherapy, radiation, laser or surgical treatments. Hairy leukoplakia (23%) was seen almost exclusively on the lateral borders of the tongue, with one case on the buccal mucosa. All but one patient had superimposed candidal infections or a history of candidiasis. Treatment could include anti-fungal and/or anti-herpetic drugs, although lesions seem to regress and recur independently. Gingival and periodontal problems (20%) included gingival pain resembling acute necrotizing ulcerative gingivitis (ANUG) and accelerated deterioration of pre-existing periodontal conditions. Acute infections required antibiotic therapy, but gentle debridement and careful scaling and root planing eliminated most problems. Stomatitis (12%), seen here as a chronic infection, can be painful and debilitating. Herpetic gingivostomatitis, on the keratinizing and non-keratinizing mucosa, was treated with anti-herpetic drugs and major apthous ulcerations responded to topical antibiotics. No oral manifestations were seen in 12% of the patients.

F.3.6 The Value of Liver Biopsy in the Diagnosis of Mycobacterial Infection in AIDS Patients

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Sixty-five liver biopsies(Lvbx) from patients with AIDS were reviewed. We analyzed pathological(path), microbiologic culture(Cx) and liver function tests (LFTs). Biopsies were divided into 3 groups: Group(Gp) A(23 pts) had positive path and/or Cx for acid fast bacteria(AFB) in the Lvbx(all M.avium-intracellulare[MAI]); 13/26(56%) had granulomata(10 were poorly formed), 7/23(30%) had hepatitis, both portal and lobular. Gp B(18 pts) having negative AFB on path and Cx in liver but Cx positive in bronchial fluid(13),blood(3),lymph nodes(3), bone marrow(2),urine(1),spleen(1) and colon(1). Fourteen pts had MAI,3MTb, 1 M.gordonae and 1 M.kansasii. Poorly formed granulomata were seen in 2 and hepatitis in 16. Gp C(23 pts) had no evidence of AFB from any site(13 Lvbx with hepatitis,4 with granulomata,1 with lymphoma and 5 normal). The mean±S.D. for alkaline phosphatase was 643±711,195±239 and 241±190 mU/ml for Gp A,B and C, respectively. There was a significant difference between alk. phos. in Gp A and Gp B($p<.02$) and Gp A and Gp C($p=.0148$). There was a significant association between granulomata and AFB in Lvbx($p<.001$). Mycobacteremia was associated with AFB in Lvbx($p<.01$), but in 5/17(29%) in Gp A blood Cxs were negative and thus would not have indicated the presence of AFB disease. The yield of AFB was 15/30(50%) in blood,23/41(56%) in Lvbx and 26/31(83%) in bronchial secretions. Lvbx was helpful in the management in 32/65(49%) of pts.

We conclude that Lvbx may speed the diagnosis of disseminated AFB(in 13/23 the diagnosis was rapidly evident on path). Granulomata on Lvbx, albeit poorly formed, and elevated alkaline phosphatase were both strongly associated with AFB in the liver.

Immunology—Immunopathogenesis

F.4.1 Influences of Related Retroviruses on Human Lymphocyte Functions
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Infection with the human immunodeficiency virus (HIV) can lead to profound perturbations of the immune system as well as to clinical disease. In contrast, two related retroviruses, the human lymphotropic virus type IV (HTLV-IV) and the Simian lymphotropic virus type III (STLV-III) have not been associated with clinical disease in their infected hosts. In this study, these viruses were grown up in the Hut-78 cell line, concentrated, band-purified and disrupted. Protein-rich preparations of these viruses were compared for their influences on functions of B- and T lymphocytes of healthy, HIV-uninfected donors. As described previously, the HIV protein preparation could induce a T-dependent, polyclonal response in B lymphocyte cultures resulting in immunoglobulin secretion. In contrast, the other two viral preparations did not cause either proliferation or differentiation of normal B lymphocytes. Pokeweed mitogen-induced B cell differentiation responses were inhibited in a dose-dependent manner with HIV but minimally with HTLV-IV or STLV-III. None of the viral preparations induced a blastogenic response in peripheral blood lymphocyte cultures. T lymphoproliferative responses to mitogens, antigens and allo-antigens were inhibited somewhat inconsistently and to varying degrees by these viral preparations, but most regularly with HIV. These findings suggest that these viruses differ in their capacity for causing immunologic dysfunction.

F.4.2 Homologous Peptides From HIV P41 and HLA CLASS II Bind CD4 on Human T Cells
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The CD4 molecule has been identified as the receptor for HIV envelope protein. Recently, the possible natural ligand for CD4 on antigen presenting cells has been localized to the β-1 domain of MHC class II. It was postulated that the MHC class II and HIV bind the non-polymorphic CD4 via similar conserved regions. A hydrophilic septamer was identified displaying a high degree of homology between p41 of HIV and the β-1 domain of HLA-DR and -DQ. Both the HIV and MHC class II derived septamers were synthesized. Incubation of these peptides, but not control peptides, with CD4 positive cells at 37°C for 45 min resulted in reduced binding of anti-CD4 antibodies (OKT4, OKT4a, Leu3) to the cells. This reduction of binding to CD4 could be blocked in the presence of chloroquin. Binding of antibodies directed against other surface antigens, were unaffected by pre-incubation with the peptides. The temperature requirement and sensitivity to chloroquin suggest that the peptides induced partial modulation of the CD4 molecules via receptor mediated endocytosis. In addition, flow cytometry showed that biotinylated chicken albumin conjugates of the peptides can bind directly to CD4 bearing CEM cells, but not to a CD4 negative CEM mutant or to B cell lines. This binding could be partially inhibited in the presence of mouse monoclonal anti-CD4 antibodies. In addition, solubilized CEM membranes were passed over a column of immobilized HIV-derived peptide. The bound material which was eluted with the soluble peptide contained a 57,000 dalton material which was positively stained with OKT4 + OKT4a reagents using Western blot analysis. These findings suggest that, the homologous regions of HIV and MHC class II, which we have identified, may be the sites involved in binding of AIDS virus and MHC class II antigens to CD4 on human T cells.

F.4.3 HLA-DR is Involved in the HIV Receptor
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Cells procured from human tissues that can be infected with HIV express both the CD4 molecule and major histocompatibility class (MHC) class II antigens. We therefore, investigated the interaction of HIV with cell surface CD4 molecules and (MHC) II antigens. Exposing whole virus preparations for 15 min to a cultured T lymphocyte line and phytohemagglutinin (PHA) stimulated peripheral blood lymphocytes (PBL) resulted in a decrease in the CD4a epitope and in HLA-DR cell surface antigens while HLA-DP and HLA-DQ increased or remained unchanged. After 120 min of virus exposure, the CD4a epitope remained diminished while HLA-DR returned to the levels of detection found on cells not exposed to virus. The specific portion of HIV that binds the CD4 molecule has been shown to be the large envelope protein, gp120. When immunopurified gp120 was added to PHA stimulated and unstimulated PBL, the CD4 epitope decreased in the same manner as was observed with whole virus preparations. However, in contrast to the binding of whole virus preparation, HLA-DR expression increased after 15 min of exposure to gp120. These studies show that HLA-DR and the CD4 molecule are involved in the receptor for HIV binding and suggest a dynamic role for a CD4-HLA-DR complex in HIV attachment to target cells.

F.4.4 Altered IL-2 Gene Expression in HIV Infected Peripheral Blood CD4+ Lymphocytes: Possible Mechanism for Virus Induced T Cell Death for the Immunopathogenesis of AIDS
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The peripheral blood lymphocytes of patients infected with HIV exhibit a variety of immunologic abnormalities the most consistent being a decrease in the number and function of CD4+ T lymphocytes. Several mechanism have been postulated to account for this defect HIV envelope protein induced cell fusion, and the intracellular accumulation of non-integrated viral DNA. The present study was designed to determine the effects of HIV infection on IL-2 gene expression in CD4+ peripheral blood lymphocytes. IL-2 production, a protein since this protein plays a central role in T cell growth and differentiation. Purified peripheral blood CD4+ lymphocytes were infected with HIV and maintained in culture for 14 days. Non-infected cells were maintained in culture as a control. On various days following infection cells were removed and stimulated for 12-18 hours with PHA/PMA. These cell cultures were assayed by FACS analysis, in situ hybridization and northern blot hybridization. CD4+ cells infected with HIV progressively lost the CD4 antigen, while retaining CD3 reactivity with virtually all cells being CD3+/CD4- by day 14. Northern blot analysis revealed that cells infected with HIV underwent a progressive and marked reduction in IL-2 gene expression. In contrast the expression of the IL-2 receptor on several other cellular genes was not altered by HIV infection. This pronounced inhibition of IL-2 gene expression induced by HIV infection may contribute to the death of CD4+, the lymphocytes in patients with AIDS.

F.4.5 A Synthetic Peptide Homologous To HIV gp120 Envelope Glycoprotein Inhibits IL-2 Production.
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We have chemically synthesized a peptide homologous to sequence 304-321 of the HIV gp120 envelope glycoprotein. Peptide 304-321 was found to decrease the production of IL-2 of a gibbon cell line MLA-144. Phytohemagglutinin-induced IL-2 production by normal human peripheral blood mononuclear cells was also reduced in the presence of peptide 304-321. Incubation of the IL-2 dependent murine CTLL-2 with peptide 304-321 resulted in a decrease in the uptake of ^{3}H-thymidine, whereas control peptides have no effect. HIV peptide-induced inhibition of CTLL-2 proliferation could be partially restored by addition of exogenous IL-2. Peptide 304-321 had no effect on the expression of IL-2 receptor (IL-2r) since peptide-treated and -untreated cells express comparable amount of IL-2r as detected by immunofluorescence using a monoclonal antibody to IL-2r. These data together with recently published results on viral induced-immunosuppresion support further studies in the role of HIV envelope glycoprotein in the immunodeficiency observed in AIDS.

F.4.6 PERIPHERAL BLOOD ADHERENT CELLS FROM AIDS PATIENTS INHIBIT NORMAL T-CELL COLONY GROWTH THROUGH DECREASED EXPRESSION OF INTERLEUKIN 2-RECEPTORS AND PRODUCTION OF INTERLEUKIN 2.
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Colony formation in semi-solid media from peripheral blood T-cell colony-forming cells (T-CFC) of AIDS patients is extremely impaired. To define whether the low plating efficiency is due to inhibition mechanisms or/and to decreased clonogenicity of T-CFC, patients' peripheral blood mononuclear cells (PBMC) were fractionated into T-cell enriched and T-cell depleted subpopulations. Both cell fractions failed to generate T cell colonies although colony growth could be obtained from unfractionated PBMC. In 5 out of 12 AIDS patients, adherent cell-depletion of PBMC enhanced the plating efficiency. Moreover, patients' but not normal adherent cells could inhibit normal T-cell colony growth in a dose-dependent manner. Media conditioned by patients' unstimulated adherent cells (LCM-A^{+}p) also inhibit normal T-cell colony formation. In addition, LCM-A^{+}p could inhibit interleukin 2-receptor (IL2-R) expression and Interleukin 2 (IL2) production by normal mitogen-stimulated T cells. These LCM-A^{+}p did not contain detectable reverse transcriptase activity or could not infect the Human Immunodeficiency Virus (HIV)-permissive T-cell line CEM. Conversely, this adherent-cell-derived inhibitory activity could be abrogated by both heating and treatment with proteolytic enzymes. These findings indicate that the low T-cell colony formation in some AIDS patients could be due to inhibitory adherent cell-derived activities.

F.5.1 Confidentiality and the Duty to Protect: The Limits of Autonomy in the Case of AIDS

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Autonomy--the right to control one's own life, including the right to privacy--is a basic ethical principle. In the case of HIV infection, which can be transmitted through sex and blood to others, autonomy comes into conflict with the harm principle--the obligation to prevent harm to others. There are both legal duties to protect third parties placed at risk by a person with HIV infection and moral duties, and the two are not necessarily coextensive. This paper explores the moral duties, in comparison to the legal ones. It presents an ethical framework for guiding physicians and health care providers, public health officials, and others who have knowledge of a person's HIV infection. The paper considers clinical, residential or institutional, and public settings. It addresses such questions as: How ought physicians and health care providers respond when HIV-infected individuals refuse to notify their sexual or drug-using partners? What are the moral, professional, and social costs of breaches of confidentiality, compared to the possible benefits of notification? What kinds of public health program can protect the interests of those already infected, those who may be infected, and those currently at risk?

F.5.2 Ethical Dilemmes Inherent in HIV Antibody Testing Legislation: A One Year Retrospective

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In November, 1985, the Wisconsin Legislature enacted unique legislation, protecting the confidentiality and rights of persons with HIV infections while protecting the public's health by requiring HIV antibody-positive case reporting. Provisions include HIV testing informed written consent procedures, a specific listing of persons to whom test results may be disclosed, reporting of positive, validated test results to the state epidemiologist, restrictions on the use of antibody test results for insurance underwriting and employment, and civil and criminal penalties for unlawful disclosure.

Ethical dilemmas faced by the bill's drafters were the following: 1) Would confidentiality/consent procedures and reporting requirements deter physicians from testing? 2) Would reporting of antibody-positives deter individuals from seeking testing? 3) Would physicians comply with reporting requirements?

Data collected from alternate sites and Wisconsin's public health laboratory were analyzed one year post implementation to determine antibody testing practices, patterns, and reporting efficacy. Of the 4,487 antibody tests performed, 57% were from private physicians, indicating their willingness to participate in the program and the willingness of at-risk individuals to be tested without anonymity. Of persons tested by private practitioners, 4.6% were western-blot positive, compared to 7.5% positivity for those tested at alternate sites. The reporting requirement of the new law may have encouraged higher risk individuals to seek enonymous testing. Use of alternate sites and private physicians has increased steadily, irrespective of the legislation. Of the 117 positives tested by private physicians, 71% (83) were reported to the state epidemiologist. Compliance is adequate for first year implementation.

Public policy makers need to consider the effect that HIV antibody testing legislation will have on encouraging at-risk individuals to seek testing, counseling, and medical supervision. Wisconsin data indicate that such legislation did not deter individuals from seeking assistance.

F.5.3 AIDS: Transfusion and Litigation

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Concurrent with the medical disaster presented by the spread of AIDS is the filing of lawsuits by individuals who have been exposed to or have contracted AIDS through blood transfusions or use of Antihemophilic Factor VIII. The authors are currently defending approximately fifty such lawsuits.

In some instances, hemophiliacs have brought lawsuits in the form of class action, wherein the class action representative claims to represent the interest of all hemophiliacs claiming similar injuries. No Court to date has allowed this type of action; if this occurs, it would have a detrimental effect on all AIDS patients because of the invasion of privacy and interference with the physician/patient relationship.

While HIV antibody tests are now used by all blood banks and plasma centers, the number of transfusion related AIDS cases will continue to increase because of the incubation time between exposure and onset of symptoms.

Litigation is growing in tandem with reported cases of AIDS. The very future existence of non-profit volunteer blood banks is in question as insurance for AIDS lawsuits is now unavailable. The authors address the future of TAA litigation and the future question of the obligation and ethics of blood banks in contacting the recipients of blood obtained from individuals who, subsequent to blood donation, test positive for HIV antibody.

F.5.4 Anti-Discrimination Legislation and the Reduction of Social Disruption Caused by AIDS

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Extensive community fear of AIDS has led to widespread discrimination against people who have or who are perceived to have AIDS, especially in the area of employment, but also in service provision (including health and welfare services), accommodation and education. Breaches of confidentiality, invasion of privacy and violation of duty of care have also been reported.

Anti-discrimination and human rights legislation has been used in an attempt to protect the rights of those who have been subjected to AIDS-related discrimination. In some cases, pre-existing legislation has been used, in others, AIDS-specific legislation has been introduced.

Ten cases of AIDS-related discrimination are surveyed, and four cases analyzed in detail to assess the effectiveness of such legislation. By itself, legislation does not enable problems based on fear of a terminal illness or prejudice against a traditionally stigmatized minority to be resolved. Legislation, however, provides an important symbolic and statutary support for attitudinal change through education.

F.5.5 Legal and Ethical Analysis of Insurance Underwriting for AIDS

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Presents results of article which will appear in June '87 Harvard Law Review. Reviews approaches used by insurance companies to eliminate applicants at high risk for AIDS, and evaluates their legal and social impact. Concludes that insurers have legal right to exclude applicants diagnosed with AIDS or ARC. Attempts by insurers to eliminate all gay male applicants are also documented, and are shown to violate state insurance laws, recommended policy of National Association of Insurance Commissioners, and state and local law prohibiting discrimination in public accomodations. Such efforts also increase employment discrimination, decrease candor of gay and bisexual males towards physicians and sexual partners, and increase financial burden on govt. programs such as Medicare, Medicaid and public hospitals.

Use of HIV antibody test results by insurers is shown to violate laws or insurance department policies in 13 jurisdictions. Legal precedent for such laws exists in 11 states which prohibit genetic testing by insurers. HIV antibody testing by insurers is demonstrated to discourage voluntary testing, deter participation in research studies, and impede vaccine trials. Such testing also violates F.D.A. labeling of the test, omits the crucial component of counseling, and cannot be guaranteed to be confidential. Financial argument used by insurers to justify testing is shown to be exaggerated.

F.5.6 Municipal AIDS Discrimination Laws as Public Health Education Tools for Preventing HIV Transmission

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In August 1985, the Los Angeles City Council passed the nation's first AIDS discrimination law, receiving national media attention, and later created a special AIDS Discrimination Unit. Similar units have since been created in San Francisco and New York. The authors, heads of these three units, have handled hundreds of AIDS discrimination complaints in the employment, housing, education, government, business, dental and medical service areas. The vast majority have been handled without litigation due to their philosophy of early intervention and mediation of these disputes.

This paper examines the nature of AIDS discrimination disputes and how they relate to attitudinal change about AIDS. It addresses the ways in which the public's desire to obey local AIDS discrimination laws can be used as effective public health education tools for compelling citizens to learn about HIV transmission. The role of stigma and taboo are discussed as they affect early intervention and mediation of disputes. Specific cases concerning funeral societies in New York and the dental profession in Los Angeles, as well as related San Francisco cases will be studied to reveal the importance of locally-based, full-time government attorneys experienced in community organizing principles in successfully conducting such intervention.

Epidemiology—Other Retroviruses

F.6.1 Lymphadenopathy Associated Virus Type 2 (LAV2) - Seroepidemiological Study in Cape Verde islands.

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A new human retrovirus (LAV2/HIV2) was isolated from an AIDS patient from Cape Verde Islands; therefore we designed a seroepidemiological study to evaluate the presence of HIV2 infection in this country. In the main island, Praia-Santiago, 236 subjects (217 males, 19 females) were tested : 93 soldiers, 110 prisoners, 13 blood-donors and 20 hospitalized patients. In the second island, Sal, sera were taken from 144 subjects (67 males, 77 females). All sera were teated for antibodies to HIV1 (HIV1-Ab) and HIV2 (HIV2-Ab) by Elisa and confirmed by Western blot. In Sal, all sera were negative for both HIV1-Ab and HIV2-Ab; in Praia, all were HIV1-Ab ⊕ and 15/236 were HIV2-Ab ⊕ : 13 were healthy subjects (2 soldiers, 9 prisoners and 2 blood-donors) and 2 women had clinical symptoms consistent with AIDS. None were homosexual men nor drug addicts. 7/15 had previous history of sexually transmitted diseases (STD) (7 patients) or transfusion (1 patient). No significant difference was found between the 9 HIV2-Ab ⊕ and the 101 HIV2-Ab ⊖ prisoners considering mean age (29.6 years vs 27.6), previous transfusion (1/9 vs 4/101), STD (5/9 vs 40/101) or travel to other African countries (1/9 vs 3/101). 4/15 HIV2-Ab ⊕ sera were completely negative by HIV1 Elisa.

This study assessed the presence of HIV2 infection in Cape Verde islands; heterosexual contacts seem to be the predominant route of HIV2 transmission. Moreover HIV1 Elisa can miss HIV2 antibodies. Therefore blood-bank screening as seroepidemiological surveys must include, at least in Western Africa, both HIV1 and HIV2 assays.

F.6.2 Prevalence of HIV and STLV-III related human T-lymphotropic retrovirus (HTLV-IV) in several populations of Ivory-Coast, West-Africa.

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The sera from 2900 individuals were collected from January to December 1986 in six geographic areas of Ivory Coast. Sera were tested for antibody to HIV by a commercially available ELISA (Abbott). All the sera which gave a ratio sample absorbance /cut-off value over 0.80 were subsequently tested by two western-blots using either HTLV-III_B or HTLV-IV_{P289} as antigenic probes. The results indicate that both viruses, HIV and STLV-III related human retrovirus-HTLV-IV-, are widely present in Ivory-Coast. Briefly the results are as follows :

- In control populations (without any risk factor) including 300 children and 850 adults, the adult prevalences were 2.7 % for HIV and 0.4 % for HTLV-IV.
- In populations with risk factors were included :
  . 350 patients receiving multiple injections. The prevalences were 6.1 % for HIV and 1.8 % for HTLV-IV
  . 1200 individuals having multiple sexual partners (prostitutes, prisoners, ...). The prevalences were 8.9 % for HIV and 9.9 % for HTLV-IV. 2.9 % had serological evidence of exposure to both viruses.
  . 200 inpatients presenting with pulmonary infections associated with asthenia and weight loss (considered as AIDS related symptoms). The prevalences were 19 % for HIV and 8 % for HTLV-IV. 13 % had antibodies to both serotypes evidenced by reactivities to envelope glycoproteins of HTLV-III_B and HTLV-IV.

The coexistence of both HIV and STLV-III related retrovirus -HTLV-IV- in Ivory Coast will allow prospective studies providing important informations on the natural history of diseases associated with these two viruses in Africa.

F.6.3 LAV2/HTLV IV INFECTION AMONG BLOOD DONORS, MULTITRANSFUSED PATIENTS AND DIFFERENT AIDS RISK GROUPS, IN FRANCE,

A.M. COUROUCE - Ch. ROUZIOUX - F. BARIN - S. CHAMARET and the RETROVIRUS study group of the french society of blood transfusion - Paris FRANCE -

Since the discovery of a 2nd virus responsible for AIDS in West-Africa, 5 blood donors have been found LAV2/HTLV IV seropositive in different french blood banks during 1986 :

- A man from Senegal with multiple heterosexual partners
- A french man living with a LAV2 positive woman from Ivory Coast
- A french heterosexual man and I.V. drug user, having stayed in Ivory Coast.
- An heterosexual man from Ivory Coast living in France for 4 years,
- The french wife of a LAV2 positive man from Ivory Coast.

All of them have been detected thanks to a positive reaction by LAV1 Elisa. They gave unusual pattern by Western-Blot analysis (WB)= clear bands on p25 and p34 only. They were strongly positive by WB-LAV2 (Diagnostics Pasteur) and RIPA-LAV2.

In addition, a multi-Centre study has been made by Elisa LAV2 (Diagnostics Pasteur) on 1145 sera : 210 polytransfused patients, 167 hemophiliacs, 452 IV drug users, 123 subjects from Africa and 193 sera which recognized only core proteins (p18 or p25) by WB. None of them have been found LAV2 seropositive.

These results suggest a West African localisation for this second AIDS virus and a very low prevalence of this virus among blood donors collected in France.

Further studies on over 9000 blood donors are in progress.

F.6.4 Transmission of HTLV-I and HIV Among Homosexual Men in Trinidad.

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Risk factors for HTLV-I and HIV infection were evaluated among a cohort of 100 homosexual/bisexual men in Trinidad. The high seropositivity for HTLV-I (15%, a six-fold increase compared to general population rates) and the finding that duration of homosexuality and number of sexual partners were associated with increased seropositivity suggested that HTLV-I like HIV can be transmitted by homosexual sex. Forty percent of homosexuals compared to 0.19% of a general population comparison group were seropositive for HIV, and sexual contact with U.S. men was the major risk factor. Prior history of gonorrhea, a marker of sexual promiscuity, was associated with HIV seropositivity as well. HIV seroprevalence was three times higher than that for HTLV-I, suggesting that HIV is more efficiently transmitted, especially since HIV appears to be recently introduced into Trinidad while HTLV-I is endemic. Markers of altered immune status were most perturbed in 6 study subjects coinfected with HTLV-I and -III. One case of HTLV-I-associated adult T-cell leukemia (ATL) in an HIV infected homosexual raises the possibility that HIV coinfection accelerated the pathogenesis of clinical ATL. Interactions between human retroviruses may amplify their clinical effects, a hypothesis that will require further consideration in populations and in areas where multiple human retroviruses occur.

F.6.5 Emerging High Rates of Human T-Cell Lymphotropic Virus Type I (HTLV-I) and HIV Infection Among U.S. Drug Abusers (DA).

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HTLV-I is associated with adult T-cell leukemia (ATL) in Japan and in populations of African ancestry in the Caribbean basin and bordering areas including southern U.S. blacks. Endemic virus infection is observed in areas where ATL may account for >50% of adult non-Hodgkin's lymphoma. Surveys of U.S. populations document low or absent HTLV-I seroprevalence in most study groups. Following-up our finding of 16% seropositivity for HTLV-I among Queens, NY DA (JAMA 255:3133), we surveyed 963 New Jersey (N.J.) and 214 New Orleans, LA (N.O.) DA. Sera were screened for HTLV-I antibodies by ELISA and confirmed by immunofluorescence, competition and/or immunoblot.

SEROPREVALENCE BY LOCATION AND RACE

		BLACK DA			NON-BLACK DA		
SITE	(year)	HTLV-I	HIV	BOTH	HTLV-I	HIV	BOTH
N.O.	(1985)	49.3%	0.0%	0.0%	6.6%	2.6%	1.3%
N.J.	(1984)	30.2%	45.0%	15.5%	8.5%	31.0%	3.2%

Black DA were significantly more likely to be HTLV-I seropositive than whites or Hispanics. Almost 50% of black N.O. DA were HTLV-I positive but HIV was absent suggesting that HTLV-I is an older endemic virus in this population. The elevated HTLV-I infection rates in the non-black DA raise the possibility that new spread of HTLV-I is emerging as a consequence of paraphernalia sharing. There are potential public health implications of this trend including long term sequelae such as lymphomas/leukemias and neurologic diseases, heightened risk to the blood supply, and potential for adverse modification of HIV natural history from retroviral co-infection.

F.6.6 HTLV-IV and HTLV-III/HIV in West Africa

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A new human T-lymphotropic virus has been recently described from healthy West Africans. A unique feature of preliminary studies with HTLV-IV indicated that in contrast to HTLV-III/HIV it was not associated with classic AIDS or related disorders. We present data on 4,248 serum samples from Senegal, Guinea, Guinea Bissau, Mauritania, Burkino Faso, and Ivory Coast. Control, sexually active risk and disease populations including AIDS were sampled from 1985 to 1987 and analyzed for reactivity to HTLV-IV and HTLV-III/HIV by radio-immunoprecipitation and SDS/PAGE and immunoblotting. Evidence for HTLV-IV infection was found in 5 of 6 countries, however the seroprevalence rates varied markedly (1%-32% overall). Healthy sexually active risk groups demonstrated higher levels of HTLV-IV infection compared to healthy control and disease groups including AIDS. The seroprevalence of HTLV-III/HIV infection also varied from country to country and highly correlated with the rare cases of AIDS diagnosed; seroprevalence for HTLV-III/HIV was uniformly lower than that of HTLV-IV. It is not clear if HTLV-IV is a completely non-pathogenic HTLV, however the biology of this virus infection shows marked differences from that of HTLV-III/HIV and the pathogenesis of AIDS. The existence of at least two cross-reactive HTLVs in many countries of West Africa indicates the necessity for distinguishing serologic assays such as RIP-SDS/PAGE and immuno-blot analysis. Present data indicates HTLV-IV is not correlated with AIDS or other related disorders. This points out the need for health policy that will address issues of prevention and control for T-lymphotropic viruses of differing oathogenicity.

Virology—Animal Models

F.7.1 Infection of Rhesus Macaques with HIV-2.

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We have attempted to infect rhesus macaques with four different isolates of human immunodeficiency virus type 2 (HIV-2, originally called LAV-2). Eight macaques, ranging in age from 18 months to 5 years, were given intravenous injections of cell-free virus using the ROD and MIR isolates. Fourteen weeks after inoculation, three animals received a second injection of virus. At time of rechallenge, one rhesus had serum antibodies to env gene products, gp140 and gp34, which we detected by immunoblot and radioimmunoprecipitation assays. Within 7 weeks of the second inoculation, two other macaques had seroconverted with antibodies to gp34 and gp140; however, virus had not been isolated up to 9 months after the initial injection of virus. More recently, two additional HIV-2 isolates, EHO and DIA, were each injected into one rhesus 3 days after xenogeneic stimulation of the animals with 10^7 human lymphocytes. Virus was isolated from peripheral blood mononuclear cells of the rhesus that received EHO at both 2 and 4 weeks after inoculation, but serum was antibody negative both times. These data suggest that the EHO strain of HIV-2 may be more infectious for macaques than other isolates tested. We have injected EHO recovered from rhesus PBMC into additional animals to determine whether infections can be established readily with this strain of HIV-2. A model system using macaques and the human virus HIV-2 would be extremely important in developing a vaccine against HIV, since a wider range of experimental vaccines could be tested than is feasible with the more limited chimpanzee-HIV system.

F.7.2 Response of Pig-tailed Macaques to SIV/SMM Infection

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A pig-tailed macaque, inoculated IV with SIV/SMM, developed a viremia that persisted until death 14 months post-inoculation (PI). The animal had chronic diarrhea, lymphadenopathy, lymphopenia and thrombocytopenia and terminally was anemic and ataxic. Autopsy revealed emaciation (22% wt. loss) and generalized lymphadenopathy and splenomegaly. Histology revealed lymphoid depletion and multinucleated giant cells in lymph nodes, spleen, intestine, brain and most other tissues. The animal also had cryptosporidiosis, and retrovirus was isolated from multiple tissues, including the brain. Blood transfusions from this animal to 3 other macaques resulted in acute disease in all 3 recipients. Two of these died at 7 and 9 days PI and the third is recovering from a clinical disease that included diarrhea, weight loss, anemia, thrombocytopenia and oral candidiasis. Animals which died had generalized lymphadenopathy, splenomegaly and hyperplasia, hemorrhage and necrosis of lymphoid tissue of the intestine. Histologically, lymphoid tissues were reactive and contained foci of necrosis and multinucleated giant cells. Bacterial organisms were not isolated or demonstrated by special stains in tissue sections. Three additional macaques were inoculated with a retrovirus isolated from either the initial case or a transfusion recipient. All 3 developed acute disease within 5 days and died within 7-8 days PI. Lesions in all 3 animals were identical to those seen in the transfusion recipients. These observations suggest that SIV/SMM is more pathogenic in the pig-tailed macaque or that the virus has become more virulent after passage in one animal (supported by NIH grant no. RR-00165).

F.7.3 Natural and Experimental Infection of Macaques With the Simian Immunodeficiency Virus

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Three of 848 macaques (0.35%) of the NERPRC colony had antibodies to simian immunodeficiency virus (SIV); SIV has now been isolated from these three macaques (two Macaca mulatta and one Macaca fascicularis). Analysis of stored sera and earlier studies have revealed six additional macaques, now dead, who previously were infected naturally with SIV while at NERPRC. Three of these six had lymphoproliferative syndromes/lymphomas. SIV was also isolated from two of these macaques. In one case, in utero transmission was documented. A total of 16 juvenile rhesus macaques have been inoculated with SIV grown in human peripheral blood lymphocytes or in HUT-78 cells. Eight of the macaques died 129-352 days post-inoculation with a variety of clinical and pathologic findings paralleling those of AIDS in humans. The other eight macaques became persistently infected for prolonged periods; these eight macaques remain alive 537-820 days post inoculation despite the continued ability to isolate SIV and persistent lymphadenopathy. The ability to survive infection correlated directly with the strength of the antibody response. There was no correlation of the dose of virus inoculum with either the strength of the antibody response or clinical outcome. Antibodies readily detected by ELISA and by immunofluorescence have been induced in macaques by ISCOM and inactivated virus vaccines; these antibodies recognized the 160/120 kd presumed envelope protein. Vaccinated macaques were not protected against persistent infection by intravenous inoculation of SIV. Additional vaccinations using larger amounts of column purified SIV are in progress in order to define conditions needed to achieve protective immunity.

F.7.4 Expression of Human Immunodeficiency Virus Long Terminal Repeat in Transgenic Mice.

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Transgenic mice were constructed that contain the human immunodeficiency virus (HIV) long terminal repeat (LTR) driving the bacterial enzyme chloramphenicol acetyl transferase (CAT). Independently derived transgenic animals showed a consistent tissue pattern of high CAT expression in thymus, heart, tail, and lens epithelium; intermediate CAT levels in spleen; and no CAT activity in brain, liver, lymph nodes, monocytes, and peripheral blood lymphocytes (PBL). Peritoneal macrophages, stimulated in vitro by supernatants from activated murine lymphocytes, showed an 8-fold increase in CAT expression when compared to unactivated cells. When T-lymphocytes from transgenic animals were propagated in the presence of IL-2, a 10-fold increase of CAT activity over unstimulated T-cells was seen. In addition, the stimulated T-cells exhibited an approximately 5-fold further augementation of CAT activity when infected with human adenovirus type-5 or herpes simplex virus type-1. These results show that tissue, immunologic, and virologic factors influence expression of the HIV LTR in these animals. This transgenic mouse system represents a safe and potentially valuable method of evaluate the effects of cellular and viral transactivators on dormant HIV proviruses.

F.7.5 The Isolation of a T-lymphotropic Lentivirus from Cats with an Immunodeficiency Syndrome

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A lentivirus, highly tropic for T-lymphocytes, has been isolated from FeLV negative cats with an immunodeficiency-like syndrome. A lentivirus present in the blood or plasma of 3 affected cats was passaged into specific pathogen free (SPF) kittens and then into cultures of ConA and Il-2 stimulated cat lymphocytes. Virus from infected SPF kittens or cultures has been injected into a larger number of SPF kittens, some having been now observed for more than 10 months. Infected kittens developed a transient fever and leukopenia several weeks after inoculation. This was followed by a generalized lymphadenopathy persisting for months.

Disease seen in naturally infected cats appeared 1/2 to 4 years or more after infection. At this stage, generalized lymphadenopathy was not as pronounced, but chronic infections of the nasal cavity, conjunctiva, gums, intestines, skin, ears, and sometimes nervous system, were prevalent. Affected animals survived in ill-health for months or years before dying. Anemia was seen terminally in some naturally and experimentally infected cats.

The virus is widespread among cats but is infectious only after prolonged and intimate contact. The feline lentivirus appears antigenically and genetically distinct, but structurally and morphologically similar, to HIV and other animal lentiviruses. Serologic tests confirmed a strong relationship between this virus infection and acquired immunodeficiency. This is the first animal lentivirus other than those of Old-world primates that has been T-lymphotropic and associated with acquired immunodeficiency-like syndromes.

F.7.6 Evaluation of an HTLV-III gp120 Prototype Vaccine in Chimpanzees

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Currently, the only known experimental animal reproducably infectable with human immunodeficiency virus (HIV) is the chimpanzee. We have inoculated chimpanzees with a prototype subunit vaccine consisting of the 120,000-dalton external outer envelope protein of HTLV-IIIb. The gp120 was purified from detergent extracts of membranes of HTLV-IIIb-infected H9 cells by immunoaffinity chromatography as previously described (Robey, et al. PNAS 83: 7023, 1986). Experimental animals inoculated with the gp120 prototype vaccine developed antibodies which precipitated the gp120 and neutralized HTLV-IIIb in in vitro infectivity assays. The chimpanzees received 4 inoculations, 50 ug each, of gp120 prototype vaccine. All chimpanzees were found to have antibodies to gp120 as detected by ^{125}I-gp120 radioimmune precipitation assays and neutralizations of HTLV-IIIb in vitro infections. Antibody to the major core antigen, p24, was not detected in the vaccinated chimpanzees indicating the purity of the gp120 vaccine preparation. HTLV-IIIb viral stocks have been prepared and titered in vitro and, after in vivo infectivity titration in chimpanzees, will be used to challenge the vaccinated animals. If the vaccinated animals can resist challenge with the homologous virus, challenge with a heterologous virus will be evaluated.

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Prevention/Public Health—Monitoring Changes in Sexual Behavior

F.8.1 Self-Reported Behavioral Change in Homosexual Men in the San Francisco City Clinic Cohort

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Although studies have documented recent declines in high-risk sexual behaviors in homosexual men, none have used information collected before the AIDS epidemic as a baseline for assessing behavioral change. Of 125 men who answered questions regarding their sexual practices in 1978, 1984, and 1985, 90% had reduced their number of nonsteady partners between 1978 and 1985. The number of nonsteady partners decreased from a median of 16 in the previous 4 months in 1978 to 1 in 1985. Comparison of men who decreased their number of nonsteady partners between 1978 and 1984 with those who did not showed no demographic differences between the groups. Exposure risk from insertive and receptive anogenital and orogenital contact declined significantly between 1978 and 1984, although anogenital contact failed to decline further in 1985. Overall decline for orogenital contacts, while significant, was not as dramatic. Comparison of long-term negatives (52% of sample) with men who seroconverted between 1978 and 1984 (41% of sample) showed that seroconvertors were younger (mean=28 years) than long-term negatives (mean=33 years). Both groups significantly decreased their number of nonsteady partners and their participation in high-risk sexual practices. The groups did not differ in their decrease in these activities over the 7-year period. While these dramatic declines provide an indirect and positive evaluation of risk-reduction educational programming, in 1985, some men continued to engage in high-risk behaviors. These data emphasize the need to characterize men who have and have not changed their behavior in response to the AIDS epidemic.

F.8.2 Prevention of HIV Infection Among Gay and Bisexual Men: Two Longitudinal Studies. Co-Authors: L. MCKUSICK, THOMAS J. COATES, J.A. WILEY, S.F. MORIN, R. STALL, University of California, San Francisco, School of Medicine. This presentation will focus on levels of high risk sexual behavior and predictors of compliance to safe sex guidelines among gay and bisexual men in San Francisco. The first cohort is a sample of 700 men recruited for participation in 1983 and 1984 as the epidemic was just beginning in San Francisco. The San Francisco Men's Health Study is a population-based sample of 843 single men from the 19 census tracts in San Francisco with the highest cumulative incidence of AIDS in 1984. They have also lowered significantly rates of participation in dangerous sexual activity. As of May, 1985, approximately 25% of the cohort were still engaged in at least one high risk sexual act per month which involved sex outside of a primary relationship. Our most recent analyses of predictors of levels of high risk sexual activity, cross-validated in both cohorts, identified 8 variables to be significantly related (R= .47, p is less than .001) to sustained low risk activity in a multiple regression analysis. Personal efficacy (the belief that one is capable of making recommended changes), was most powerfully associated with level of risk activity. Men in relationships were also found to be engaged more frequently in behavior that might transmit HIV than men not in relationships. Depression was greater in those who subsequently reduced risk. Younger men were more likely to be engaged in high risk activity and level of agreement with risk reduction guidelines was related to low risk activity. Denial of the virulance of the epidemic was related to continued high risk activity. Holding a visual image of AIDS deterioration was related to low risk activity. Finally, levels of both drug and alcohol use during sexual activity was related to non-compliance with safe sex practices.

F.8.3 Condom Use in a Cohort of Gay & Bisexual Men

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Between 5/1/86 and 12/1/86 503 gay and bisexual men enrolled in a prospective study of HIV infection were surveyed concerning their attitudes and use of condoms. 328 (65%) reported at least one episode of anal intercourse during the 6 months prior to the survey and constitute the study population. Most men were non-monogamous with 72% reporting 2-100 sexual partners in the last 6 months. 24% reported half or more of their sexual partners were anonymous. Although a majority (90%) endorsed the belief that condoms can "reduce the spread of AIDS," 62% stated that they "never" or "hardly ever" wore a condom during anal intercourse in the last 6 months and 64% stated that their partners "never" or "hardly ever" wore condoms during anal intercourse. 8% of the men reported a past experience of condom breakage but the majority indicated this happened only once. 5% reported a past experience of condom slippage, usually before ejaculation; but again most (60%) related that this was rare or happened only once. Factors involved in the underutilization of condoms in this population may relate to the following surveyed perceptions: condoms spoil sex (22%); purchasing condoms is embarrassing (18%); using condoms "turns off" partners (16%); condoms are not readily available (22%); or condoms are only used by "straights" (26%). Their underutilization is probably not related to deficits in knowledge since 91% identified receptive anal intercourse as the highest risk sexual activity vis-a-vis AIDS transmission. Also, the fact that 35% reported that they were "high" on alcohol/drugs with half or more of their partners may contribute to this underutilization. Finally, this underutilization may relate to the relatively low incidence of AIDS in Pittsburgh, and the fact that 60% of our group did not personally know someone with AIDS.

F.8.4 Changes in Sexual Activities Among Participants in the Multicenter AIDS Cohort Study

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4,955 gay/bisexual men were enrolled in a prospective study of the natural history of HIV infection. Data on self-reported sexual activities were collected at four 6-month intervals beginning in April, 1984. We observed a study increase in celibacy (2% → 12%) and monogamy (12% → 27%) and a decrease in number of partners. In general, there was a reduction in all high risk behaviors; the proportion not practicing receptive anal intercourse increased from 26% to 49%. Fisting was uncommon at baseline and has become a rare practice. Use of douches/enemas has declined markedly. At baseline, 66% of MACS participants reported use of nitrite inhalants; this proportion had declined to 44% at the fourth visit.

The use of condoms with anal sex (either receptive on insertive) doubled over the course of 4 visits, but still less than one-third reported using condoms with anal sex. The direction and magnitude of reported changes in activities varied modestly when stratified by race, age, city, education or HIV antibody status. We do not now have data to determine whether our participants are becoming more selective in choosing partners who have similar serologic status. We will present information on behavior changes through five visits.

These data demonstrate a marked and continued decrease in sexual practices that increase risk of HIV infection. However, further reductions are clearly warranted. Safe sex education programs must be improved, expanded and sustained.

F.8.5 Declining incidence of sexually transmitted diseases as a result of an AIDS-prevention campaign.

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An AIDS-prevention campaign especially directed towards homosexual men started in the Netherlands in 1983. This campaign was nationwide but a special effort was made in Amsterdam. To see what influence this campaign had on the lifestyle of homosexual men, we studied rectal (RG) and homosexually acquired (HAG) male cases of gonorrhoea treated at the STD-clinics of the Municipal Health Service:

year		1981	1982	1983	1984	1985
male cases	total	3,407	3,139	2,837	2,380	2,051
of	RG (%)	451 (13.2)	502 (16.0)	471 (16.6)	271(11.4)	218 (10.6)
gonorrhoea	HAG (%)	1,060(31.1)	1,137(36.2)	1,013(35.7)	570(23.9)	435 (21.2)

The incidence of syphilis among men in Amsterdam was in 1981 108, in 1982 110, in 1983 101, in 1984 91,5 and in 1985 53 per 100,000.
From these data we conclude that homosexual men in Amsterdam changed their sexual lifestyle since 1984.
Data from 1986 will be presented at the conference.

F.8.6 Use of an AIDS Hotline as an Educational Tool as well as a Measure of Effectiveness of Outreach Efforts.

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HERO has conducted an AIDS information and referral hotline since 1983. A record of each call was kept, and analysed to identify trends, to characterize the different types of caller, and to categorize the type of information asked or advice sought.

This analysis demonstrated that the hotline was primarily an information tool, rather than a crisis or counseling service. In order of frequency, callers were gay white males (33.7%), straight white females (28.3%), gay black males (10.5%) and straight black females (8.5%). The majority of calls (53.3%) were for general information on AIDS; 14.3% of calls were for referrals to antibody testing sites, 8.1% asked symptoms of AIDS, and only 2.1% of callers were seeking counseling.

Analysis of calls after subsequent targeted outreach efforts by HERO to specific groups (minorities, IV drug users) indicated an increase of calls from these groups. This suggests that tracking of hotline calls can be used to help evaluate the effectiveness of outreach efforts.

Immunology—Viral Replication

F.9.1 Mononuclear Phagocytes and Accessory Cells in the Pathogenesis of AIDS

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Several lines of evidence indicate that, in vivo, cells other than $T4^+$ lymphocytes harbor HTLV-III/LAV. Using a number of different methods, extensive studies of brain, lung, lymph node and skin tissues from HTLV-III/LAV-positive individuals clearly established that the virus-positive cells belong to the mononuclear phagocyte lineage. In brain tissue the virus-positive cells exhibited characteristics of monocyte/macrophages, in the lung they were mainly alveolar macrophages, in the lymph nodes they were the follicular dendritic cells and, in the epidermis, the Langerhans cells were HTLV-III/LAV positive. In vitro virological studies using monocyte/macrophages as targets demonstrated that these cells are highly susceptible to and permissive for the virus, particularly those isolates which were recovered from cells of the mononuclear phagocyte lineage. The longevity of virus production, the cytopathic effect and the presence of infectious virus particles within vacuoles indicates that these types of cells represent not only targets for HTLV-III/LAV, but perhaps more importantly, they are the primary source of virus persistence in vivo. Moreover, the normal physiological role of mononuclear phagocytes strongly suggests that these virus-infected cells are responsible for virus dissemination. The biological properties as well as the nucleic acid analysis of several isolates recovered from various types of cells from the mononuclear phagocyte lineage will be discussed.

F.9.2 Cytokine Regulated Control of HIV Expression in Chronically Infected Promonocyte Clones

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Cells of the monocyte/macrophage lineage have been implicated as major targets of HIV infection. In order to further study this phenomenon, the promonocyte cell line, U937, has been used as a model for monocyte infection. Following HIV infection of U937 cells, chronic low-level virus-producing clones can be isolated which do not manifest a cytopathic effect and which contain integrated HIV proviral DNA copies. Clones such as these permit the detailed study of factors which might regulate or influence HIV expression. Our findings have shown that T cell and monocyte derived factors can control virus expression in these chronic HIV-producing clones. The T cell lymphokine, granulocyte-macrophage colony stimulating factor, can increase HIV production in one clone, U1, by 3 to 4 fold. Another lymphokine, gamma interferon, produces the opposite effect by inhibiting virus production. Monokines derived from LPS induced macrophages were shown to strongly up-regulate HIV production in these clones. The purified monokine, IL-1β, has been tested for viral regulatory properties in U1. Even though recombinant IL-1β had no effect on HIV expression, antibody to IL-1β inhibited the enhanced expression of HIV in U1 by other factors. Interestingly, following factor induction IL-1β mRNA was up-regulated 20 fold in U1 over uninfected U937 cells. This implies a regulatory role for IL-1β in controlling HIV expression in this chronic HIV-producing clone and suggests that the inductive signals for virus expression by other external factors involve IL-1β in the final common pathway.

F.9.3 Quantitative Cytofluorographic Analysis of HIV Infected Macrophages (MΘ): Removal of CD4 Positive Lymphocytes Through a Cell Fusion Process

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It is unlikely that HIV infection of CD4 lymphocytes alone can fully explain the immune dysfunction observed in AIDS. MΘ infected with HIV may directly cause AIDS by serving as a virus reservoir and by removing CD4 T lymphocytes through an HIV envelope glycoprotein mediated fusion process. Quantitation of cell surface and cytoplasmic antigen in infected cells has been difficult using conventional immunofluorescent staining of cells on slides. We have developed a system which permits maintenance and differentiation of human peripheral blood monocytes in suspension culture for prolonged periods of time. This allows quantitation of CD4 and/or HIV antigens on single infected and uninfected MΘ by two color immunofluorescent cytofluorographic analysis. These studies have shown: (1) CD4 antigen is present on monocytes, with antigen expression showing marked donor variability (28-85% of cells). (2) Both OKT4 and OKT4a epitopes are present at equivalent levels on MΘ. (3) CD4 antigen density increases tenfold during the first 1-2 weeks of culture. (4) Cultured MΘ between 2 hours and 57 days of age can be infected with HIV. (5) HIV p24 antigen is present in up to 70% of infected cells. (6) HIV infected MΘ frequently form multinucleated giant cells with poor adherence characteristics. (7) Two color immunofluorescent labeling shows HIV infected MΘ fuse and remove CD4 lymphocytes in vitro.

F.9.4 INFECTION OF HUMAN BONE MARROW CELLS BY THE HUMAN IMMUNODEFICIENCY VIRUS (HIV).

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In order to examine whether immature T cell precursors are infectable by HIV, normal bone marrow cells were infected in vitro, before and after depletion of mature T cells with OKT3 or T11 plus complement. The culture was performed in the presence of phytohemagglutinin (PHA) and recombinant IL2 (rIL2). Five to 10% of unfractionated or T-cell depleted bone marrow cells were specifically labelled with a fluorescein-conjugated HIV preparation. The peak of reverse transcriptase activity was detected at day 15 in all cases. At this time, infected cultures of T-cell depleted bone marrow were composed of $T3^+$(50-55%), $T8^+$(50-55%) but not $T4^+$ (less than 2%) cells whereas non-infected cultures were composed of $T3^+$(70-78%), $T8^+$(15-20%) and $T4^+$(50-55%) cells. Non-infected bone marrow cells generated a relatively high number of T-cell colonies in methylcellulose (more than 100 colonies/$5x10^4$ cells at day 15) whereas for infected cells, both unfractionated and cell fractions, displayed a time-dependent impaired T-cell colony growth capacity (less than 20 colonies/$5x10^4$ cells). Phenotypic characterization of T-cell colonies obtained from infected bone marrow cells revealed the presence of $T3^+$,$T4^+$,$T6^+$,$T8^+$ cells whereas colonies derived from non-infected cells were composed of $T3^+$,$T4^+$ and $T3^+$, $T8^+$ but not $T6^+$ cells.

This model thus seems to mimic the abnormal proliferation and differentiation of T-CFC observed in patients with AIDS and Persistent Lymphadenopathy Syndrome.

F.9.5 Low Numbers of Cytotoxic/Suppressor CD8+ Lymphocytes Prevent HIV Replication in Autologous Purified CD4+ Lymphocytes

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Our studies have focused on the role of cytotoxic/suppressor T lymphocytes in the control of human immunodeficiency virus (HIV) replication in cultures of peripheral blood mononuclear cells (PMC) from HIV seropositive subjects. Previously published results demonstrated that when this T cell subset, which expresses the CD8 (OKT8/Leu2) surface antigen, is removed from PMC by cellular immunoaffinity chromatography and anti-CD8 antibodies, HIV replication is detected. Reconstitution of these cultures with the recovered CD8+cells abrogated HIV replication.

Some individuals have been identified whose PMC fail to release HIV even after CD8+ cell depletion. Analysis of this cell population revealed that it contained 10-15% contaminating CD8+ cells. To determine if these cells were sufficient to interfere with HIV replication in the PMC, we specifically enriched for CD4+ cells using anti-CD4 antibodies. The resulting population, which contained greater than 90% CD4+ and less than 5% CD8+ cells, routinely yielded high titers of HIV, while PMC depleted of CD8+ cells by negative selection as described above did not produce virus. Readdition of CD8+ cells inhibited replication of HIV, and prevented the appearance of HIV-induced cytopathology which was often evident in cultures of purified CD4+ cells.

These results suggest that most HIV seropositive individuals harbour HIV in their peripheral blood CD4+ cells, and that the efficiency of CD8+ cell control of HIV replication within this subset varies from individual to individual.

F.9.6 Immunologic Profiles of Mothers in Perinatal Transmission of HIV Infection

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HIV infection is known to infect T-helper lymphocytes and many other cells important to the function of the cellular immune system. To assess if these effects are associated with perinatal transmission of HIV, we used a fluorescent automatic cell counter to evaluate the levels of Leu 2,3,4,7,11,2H4 and 4B4 positive lymphocytes in HIV seropositive mothers who gave birth to IgM western blot positive infants, HIV seropositive mothers of HIV IgM seronegative children and seronegative control mothers who were matched for age and parity. Of the 234 mothers who delivered babies in the study group in Kinshasa, Zaire, 25 were HIV seropositive. Six of the 25 mothers had HIV IgM seropostive infants. The mothers of the IgM positive babies had a significantly lower T-helper/T-suppressor ratio (.57±.12) than the mothersof IgM negative babies (3.3± .68) $p<.001$. The mothers of IgM positive children also had significantly more T-suppressors (820±257 cell/mm3) than mothers of IgM negative babies (375±58 cells/mm3) but no differences in Leu3+2H4+ or Leu3+4B4+ cells. HIV positive mothers of IgM negative infants and seronegative control mothers had similar T-helper,T-suppressor,2H4 and 4B4 population, but the HIV positive women had signficantly lower numbers of Leu 11+ (NK) cells (33±5 cells/mm3 vs 130±14 cells/mm3) $p<.001$. HIV positive mothers who transmit AIDS to their children have inversed T-helper/T-suppressor ratio and elevated suppressor cells which are signficantly different from what is seen in HIV positive mothers who do not transmit the infection to their infants. With further study, these lymphocyte parameters may be used to judge the risk of perinatally transmitted HIV infection.

Closing Plenary Session

F.10

Chairmen: Jean-Claude Gluckman
Chairman, II International Conference on AIDS
Paris, France

Lars Olaf Kallings
Chairman, IV International Conference on AIDS
Stockholm, Sweden

Summary and Current Status of AIDS Research
June Osborn, Dean, School of Public Health, University of Michigan, Ann Arbor, Michigan.

Lars Olaf Kallings, Director, National Bacteriological Laboratories, Stockholm, Sweden.

Edward N. Brandt, Jr., Chancellor, University of Maryland, Baltimore, Maryland.

Introduction of the Secretary
Robert E. Windom, Assistant Secretary for Health, U.S. Department of Health and Human Services, Washington, D.C.

Concluding Address: AIDS -- Charge for the Future
The Honorable Otis R. Bowen, Secretary, U.S. Department of Health and Human Services, Washington, D.C.

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